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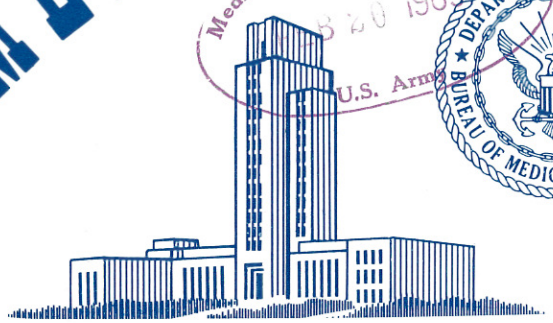
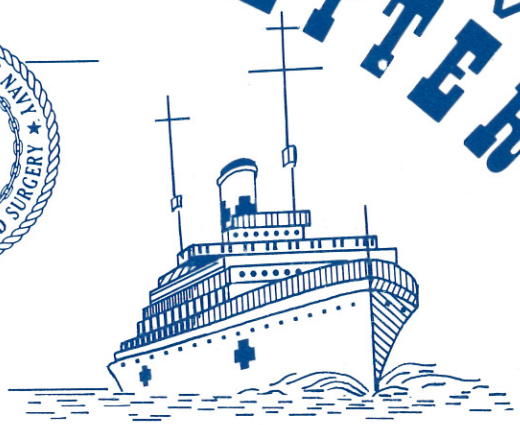
UNITED STATES NAVY MEDICAL NEWS LETTER





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Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

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COMBAT FATIGUE VERSUS PSEUDO-COMBAT FATIGUE IN VIETNAM

CDR Robert E. Strange, MC USN, Milit Med 133(10):823–826, October 1968.*

It has been established that combat psychiatric problems have been less frequent in the Vietnam Conflict than in previous wars. Experience aboard the U.S. Navy Hospital Ship REPOSE in the combat zone during 1966, however, indicated that pathological emotional reactions continue to occur, although less often than anticipated, and that their recognition and management are still important problems for the military medical officer. Those few cases of combat fatigue which are encountered must be recognized and differentiated from other similar appearing syndromes, most numerous of which are those of personality or psychoneurotic disorders developing symptoms in response to the stress of battle. This common occurrence may well be called pseudo-combat fatigue because of its superficial similarity to the classic situational combat reaction. Recognition of differences in these syndromes is necessary for the physician in making the decisions which will most benefit the patient and his military unit.

Combat Fatigue

The syndrome of combat fatigue or combat exhaustion is a very specific diagnostic category. It may be defined as the transient pathological reaction of a basically healthy personality to severe stress of combat, and is included in the American Psychiatric Association nomenclature in the category of Gross Stress Reactions. Regarding such reactions, the *Diagnostic and Statistical Manual* of the American Psychiatric Association states: "This diagnosis is justified only in situations in which the individual has been exposed to severe physical demands or extreme emotional stress such as in combat or in civilian catastrophe. . . . In many instances this diagnosis applies to previously more or less 'normal' persons who have experienced intolerable stress." Although the presenting symptom complex may vary, the following characteristics are generally present in patients with this problem: (1) past history of comparatively healthy emotional and social adjustment, (2) previously satisfactory military performance, and (3) severe and prolonged exposure to traumatic combat experience. Also, they usually have histories of marked physical exertion and fatigue, sleep deprivation, inadequate diet, and other somatic as well as emotional stress. Other authors have previously described the variable symptoms among these patients, including generalized anxiety, depression, apathy and withdrawal, conversion reactions, agitation and disorganization, and psychosomatic manifestations. Mild symptoms are normal among combat troops, and are considered to be pathological only when they become severe enough to impair the patient's ability to perform his duties effectively or persist inappropriately when the stress of combat is no longer present. In these cases diagnosis of Combat Fatigue is indicated.

Aboard the USS REPOSE, while providing medical support for Marine operations in the I Corps area during 1966, cases of classical combat fatigue as described above were relatively uncommon. This diagnosis was established in only 15 percent of the psychiatric patients hospitalized aboard the vessel, but it was considered nevertheless to represent a potentially significant loss of combat manpower. It is quite possible that this figure may not be representative of the actual incidence of combat fatigue among operational units, due to many variable selection factors operating in the admission of patients on the ship. Discussion with medical officers assigned to Marine units ashore, however, indicated a roughly equivalent case load during periods of heavy engagement. It is noteworthy that most of the patients hospitalized for combat fatigue aboard REPOSE were young men who had been in positions of considerable responsibility, most often junior non-commissioned officers, such as corporals assigned as squad leaders, or hospital corpsmen working with combat units. Invariably their military record was excellent, their past history that of healthy social adjustment, and their combat experience lengthy and harrowing. Characteristically, they had been in the war zone for more than six months, had strong emotional investment in their units, and functioned in a leadership or other responsible role. The most common symptom complexes were those of insidiously or acutely developing generalized anxiety or depression with accompanying psychophysiologic manifestations. The following is an illus-

From the U.S. Navy Hospital Ship REPOSE.

* Assistant Chief of Neuropsychiatry, U.S. Naval Hospital, Philadelphia, Pa., 19145. Read before the Section on Military Medicine, American Medical Association, Atlantic City, N.J., June 19, 1967.

trative case of this combat fatigue syndrome and its treatment:

Case 1. This twenty year old CPL USMC was hospitalized aboard USS REPOSE after approximately two weeks of out-patient supportive treatment by his battalion surgeon because of chronic anxiety, nightmares, and persistent headaches. History revealed that he was the product of an intact, happy family with no previous indications of emotional or social problems. He attended a trade school successfully and then enlisted in the Marine Corps. For two and one-half years he had served quite satisfactorily, and during the eleven months prior to hospitalization he had been assigned to combat duty in Vietnam. His competence was such that he became a fire team leader shortly after he arrived in the field, and very soon after that he was made a squad leader. Over a number of months he led his squad through many patrols, was involved in numerous fire fights and mortar attacks, and participated in several lengthy operations in which there was prolonged engagement with the enemy. During the month preceding his admission to the sick list his unit suffered heavy casualties, which included a number of his own squad members. On one occasion he sustained superficial wounds, as several of his men were seriously injured in a grenade blast. Shortly thereafter, his unit came under heavy mortar attack, this being the fifteenth such mortaring experience for the patient. He recalled that when this occurred "things seemed hopeless"; and, although he felt he should have been active among his men, he remained in his foxhole all night because "I was just too scared and tired to get out." He was then evacuated to his local field medical unit, but was immediately returned to duty because of apparent lack of overt symptoms. For two weeks he noted increasing apprehension, startability, nightmares, insomnia, and headaches; and he was seen on several occasions by his battalion medical officer and treated with analgesics and mild ataractic medication. His symptoms continued, however, and his effectiveness in his duties deteriorated. He was consequently transferred to *Repose* for psychiatric treatment, at which time he exhibited marked anxiety, with agitation, tremulousness, and pressure of speech. He was near tears and struggling to maintain emotional control. Thought content was dominated by combat apprehension and feelings of guilt both about this apprehension and the recent loss of men under his leadership. He reported sleeplessness, terrifying dreams, anorexia, and a sense of impending death. After initial examination he was treated with chlorpromazine, 100 mgs intramuscularly, and then given the same amount orally every six hours over a twenty-four hour period. He slept soundly during this time but was able to awaken for meals and self-care. The dosage of chlorpromazine was then decreased to 50mgs orally every four hours during the waking hours of the next two days, along with 75mgs in spansule form in the late evening. Initially, this was supplemented with oral barbiturates at taps, but this was soon discontinued as a normal sleep pattern was re-established. After the first twenty-four hours of heavy medication and sleep the patient was ambulatory on the ward, and his symptoms of anxiety vastly improved. His feelings of apprehension and guilt were discussed in both individual and group psychotherapy sessions, with much ventilation and abreaction, and there were support, interpretation, suggestion, and reality emphasis by the medical officer, nursing staff, and patient group. Medication was gradually decreased and then discontinued. Although he remained ambivalent about combat, there was no recurrence of anxiety symptoms, and he was returned to full duty after ten days of hospitalization. Follow-up information indicated that he served two more months under intermittent hostile fire and satisfactorily completed his tour of duty in Vietnam.

Pseudo-Combat Fatigue

The majority of psychiatric casualties in Vietnam are not the classical syndrome of combat fatigue as described above, however. These are young men with psychoneurotic or, far more commonly, personality disorders who develop overt symptoms in the environment of the war zone. Superficially their presenting symptoms may closely resemble those of the true combat fatigue patient, but their history and hospital course are quite different. At the time of their hospitalization it may be very difficult to obtain information about their current situation and history, but, when the facts become known, they most often reveal poor past adjustment. Usually there are indications of impulsivity, poor stress tolerance, tenuous emotional control, and/or previous psychiatric contacts and symptoms. Characteristically, these patients have been in the war zone less than six months, and the degree of combat stress has been less severe. They are rarely in positions of responsibility and leadership, and feelings of guilt are uncommon in their thought content. Even if these clues are not apparent, their response to the supportive but highly directive, reality-oriented

therapeutic techniques of combat psychiatry are distinctive. Because of the deep-seated nature of their problems, inadequate motivation and poor identification with their military group, these pseudo-combat fatigue patients respond poorly to treatment, although their symptoms of anxiety, despondency, or somatic complaints may seem to improve in the comparatively sheltered environment of the hospital. The crucial test is the prospect of return to duty, and at this point symptoms frequently recur, new ones appear, or the patient may for the first time frankly discuss his past emotional problems and inability to tolerate them.

Aboard USS REPOSE, 57 percent of the psychiatric admissions were diagnosed as personality or psychoneurotic disorders, and approximately 50 percent of these were hospitalized following exposure to battle stress, with symptoms differing little from the combat fatigue cases. At the time of hospitalization past history was frequently not obtainable and initial treatment was very similar to that of the true combat reactions. The following case is a typical example of this pseudo-combat fatigue syndrome:

Case 2. This twenty-two year old L/CPL USMC with two years of active duty and four months of service in Vietnam was hospitalized aboard *Repose* after he "froze" while under enemy fire. At the time of admission he was grossly anxious, tremulous, and agitated. His speech was in explosive bursts, interrupted by periods of preoccupied silence, and he reported only vague memory for the combat experiences of recent weeks and the incident which had precipitated his evacuation from the field. He was immediately treated with chlorpromazine in a dosage schedule similar to that of Case 1, and twenty-four hours later his symptoms had remarkably improved. He was calm and communicative, and a history could be obtained. This indicated long-standing problems with emotional and impulse control which had caused difficulties in social, family, and school relationships. He enlisted in the Marine Corps after impulsively quitting high school, and his two years of service had been marked by frequent emotional upheavals, marginal performance of duty, and a total of nine disciplinary actions for a variety of minor offenses. His initial two months of Vietnam duty had been comparatively peaceful. As his unit made more contacts with the enemy, however, over the next two months he grew increasingly apprehensive, and this became more severe after he received a minor shrapnel wound. On the night prior to hospitalization, he was involved in a brief but intense fire fight, and he "froze" in a state of tremulous dissociation. He was sedated, maintained in the field overnight, and then evacuated to the hospital ship in the morning. There his treatment program was very similar to that of Case 1, utilizing both chemotherapy and group and individual psychotherapy and he showed early good results, with almost complete initial disappearance of anxiety symptoms. It was noted that some tremulousness and apprehension recurred, however, whenever new casualties arrived aboard, or when combat ashore was visible or audible from the ship. He then demonstrated acute exacerbation of symptoms when confronted with the prospect of possible return to duty, and he was finally evacuated from the combat zone with the diagnosis of emotionally unstable personality after ten days of hospitalization.

Comment

Although the presenting illnesses of anxiety symptoms while under enemy fire are similar in the two patients described above, the differences are noteworthy, and demonstrate the differentiating characteristics between true combat fatigue and pseudo-combat fatigue as observed aboard USS REPOSE in Vietnam. Case 1 had previously good adjustment and lengthly combat service with severe stress; also his illness involved feelings of responsibility and guilt as much as personal fear. His response to treatment was consistent, and he remained symptom-free when faced with return to duty, even though he had ambivalent feelings about this disposition. Seventy-eight percent of the young men with this situational reaction to combat were returned to duty from the hospital ship, usually after less than fourteen days hospitalization. Case 2, although he initially appeared to have a situational syndrome of combat, demonstrated historically his poor adaptive capacity, and further indicated this in his responses to treatment and the prospect of return to the field. It is likely that he would have become a military psychiatric patient even if he had not been exposed to battle stress. This case exemplifies the most common type of psychiatric casualty in Vietnam. Approximately 50 percent of these patients were nonetheless returned to duty after hospitalization aboard the ship, but it was in this group that some failures and rehospitalizations occurred.

The principles of combat psychiatric treatment have been well described, are now well established, and have been well validated in Vietnam. They may be summarized as (1) Treatment in the combat area;

(2) Adequate sedation and replenishment of physical deprivation; (3) Ventilation and supportive-directive psychotherapy; (4) Discouragement of invalidism and (5) Attempt to return to duty as rapidly as possible. Since the Korean Conflict, the only major change in the physician's armamentarium for this treatment regimen is the present availability of phenothiazine ataractic drugs, which have proved extremely successful, as used in the case histories described above. These general techniques of early treatment can be utilized with symptomatic success in almost all combat psychiatric casualties. The medical officer is then faced with the serious problem of deciding on the disposition of these patients. It is in making this decision that accurate psychiatric diagnosis is most essential, and the few cases of true combat fatigue with their good prognosis must be differentiated from those superficially similar and much more common patients with pseudo-combat fatigue, i.e. basic personality or psychoneurotic disorders. The prognosis for a successful combat adjustment in these latter cases is much more guarded. Some of them will be able to complete their combat tour with at least limited success and should be allowed to do so, although this necessitates critical evaluation and judgment by the physician. Many of them must be evacuated out of the combat area, in order to avoid recurrence of symptoms and danger to themselves and their associates. The decision of who should be returned to duty and who should be evacuated after treatment for psychiatric symptoms occurring in combat is always a difficult one which involves many factors. Experience aboard REPOSE indicated that the single most important necessity was that of accurate diagnosis and differentiation of true combat fatigue from pseudo-combat fatigue syndromes in patients with underlying emotional disorders.

(The references may be seen in the original article.)

VOLVULUS OF THE SIGMOID—SURGICAL INDICATIONS

J. Richard Prather, MD and Ralph F. Bowers, MD, Resident Physician
14(8):39–48, August 1968.

The increased incidence of volvulus of the sigmoid colon as a cause of obstruction of the large bowel is becoming more evident as our population grows older. Drapanos and Stewart reported 88 percent of their patients were over 50 years of age, and this parallels our experience. It was noted in our study that 71 percent were above this age. Severe neurologic disease is present in most patients with this condition under 50 years of age.

Sigmoid volvulus is more common in males than in females. It is felt that the woman's abdominal wall is more relaxed and that her pelvis is wider. This gives the loops of bowel more room to move about, thus untwisting spontaneously any volvulus that may have started.

Etiology

Several anatomical features seem to predispose to this disease, although the exact cause is unknown. Probably the most important factor is a redundant sigmoid loop, either congenital or acquired. This may be due to chronic constipation or to a high residue diet with a large amount of "roughage." A long and freely movable mesocolon may also contribute to this condition. A third factor is a sigmoid loop whose limbs lie in close proximity. Congenital reasons or inflammation of the bowel wall with its resultant scarring may cause this derangement.

Pathology

Although some cases show a clockwise torsion, the twist in volvulus usually occurs in a counterclockwise direction around the axis of its mesocolon. This is accompanied with an axial torsion about the axis of the bowel. The axial torsion is always twice as great as the one of the mesocolon, as shown by Groth. An obstruction, simple or strangulated, is then caused by the torsion of the mesocolon and bowel. Mild or moderate torsion produces an obstruction which is simple, characterized by bowel distension. The sigmoid wall remains viable and gas and fluid are forced into the involved loop. Bowel contents may also be forced into the rectum

Surgical Service, Kennedy Veterans Administration Hospital, and the Department of Surgery of the University of Tennessee College of Medicine, Memphis, Tennessee.

so that diarrhea may be present along with obstruction. If this condition is not corrected in a few days, necrotic changes will take place in the bowel wall. When there is a marked degree of torsion, strangulation occurs. As the veins are occluded, venous stasis quickly ensues. Arterial obstruction takes place quite rapidly. Resultant infarction then occurs with thrombosis of the mesocolic vessels. In addition to the closed loop obstruction, the proximal large bowel may become distended. If the ileocecal valve is competent, a double closed large bowel loop obstruction takes place. Dilatation of the small bowel ocurs when the ileocecal valve is incompetent.

One simply cannot recount the various facets of indications for surgical treatment in this condition without knowledge of the pathological-physiological aspects, the fate of the untreated patient, and the problem of the acute and chronic obstruction.

With the above comments in mind, the importance of the sneaky, almost unannounced onset of the obstruction must be recognized as one compares the bowel habits of the aged to the newly achieved habit of the elderly patient with sigmoid volvulus. Constipation is traditionally a problem of the aged patient with lessened physical activity and vigor, loss of muscular tone, smaller amount of bowel residue as the older patient reduces the amount of food intake, and dehydration with lessened need for water intake as sweating diminishes. A matter of great importance may be the diminished activity of all secreting glands in the aged. The lack of alertness in the desire for bowel movement, a matter consistent with reduced reflexes, reduced pain sensation, and general inertia accompanying this less vigorous individual, contribute to this dilemma. As a patient ages, the vagaries of the normal bowel habits are indeed difficult to discern.

Consequently, slight changes consistent with large bowel obstruction, if mild, can easily be overlooked even by the most astute physician. From our cases, abnormal intermittent distention, often without too much pain, may herald the onset of the condition. Here, common sense must help to establish the indications. As the aging abdominal wall relaxes, distention or the potbelly may be the normal state for this patient. Abnormal distention is the key word and really must be established from the observation of the patient and the x-ray examination. Our experience dictates that the patient knows better than anyone else whether the distention is abnormal. Sometimes the spouse, if reliable, can add pertinent remarks about this.

A consideration of this constipation, normal to abnormal distention, and potbelly versus abnormal belly prominence is the first requisite of establishing an indication. If not, a crusading proctoscopist would place many of the undeserved elderly people in the knee-chest position for unnecessary and perhaps dangerous proctoscopy. The authors contend that the establishment of the diagnosis sufficiently to create an indication for therapy is indeed difficult and herein the danger lies. The mistake is mainly made when the physician fails to recognize the abnormality and neglects to induce action—oftentimes thinking that the old man is obsessed with bowel function now that his interest is not so positively related to organs anterior to the rectum. No monograph can instruct one how to establish this part of the indication and no profit will be gained by belaboring the point.

If the abnormality is suspected, one does a physical examination and studies the plain x-ray of the abdomen. The physical examination reveals distention, loop patterns, peristaltic waves, drum-like tympany often different pitch from the type heard in small bowel obstruction, respiratory distress varying as the pulmonary function is limited, tachycardia, and occasionally, vomiting. Often the patient does not look as ill as the degree of distention would indicate, and this is dangerously confusing.

Roentgenological Findings

In most instances, the diagnosis of sigmoid volvulus can be confirmed by a flat film of the abdomen. Often a largely distended loop of colon, containing fluid levels, arising from the pelvis, and filling most of the abdomen, is situated on the right side of the abdominal cavity.

This dilated sigmoid assumes the classic shape of a "bent inner tube" or a "large horseshoe." With progression of the disease, the proximal colon may become distended. If the ileocecal valve is incompetent, many dilated loops of small bowel may be present on the film. If this occurs, the sigmoid loop may be hidden, and the diagnosis can be quite difficult. Barium enema should be done in doubtful cases. A typical twisting at the point of obstruction giving what is called a "bird's bill" or "ace of spades" appearance may be revealed in the proximal portion of the rectum. In the cancer patient, there is a sharply cut-off margin, which is not present in volvulus. The torsion at this area has in some circumstances been released by barium enema itself. After reduction of the volvulus, a barium enema reveals a

dilated and redundant sigmoid. A large amount of barium is required to fill the loop which is very poorly evacuated.

It is helpful to recognize whether the obstruction is partial or complete; and, if complete, whether strangulation is likely. Simple enema, fluid or Fleet, may give information that suggests the need only of a bowel movement or the fact that fecal impaction is the lesion instead of volvulus. The indication for further use of proctoscopy or operation is now at hand.

Indications for Therapy in the Acute Stage

Phase I. First, the physician must at this time feel confident that volvulus is indeed present. Plain film should have been suggestive. If an enema has not corrected the condition, then further steps are necessary. It must be emphasized that an ordinary enema will often untwist a volvulus and that the diagnosis must not be cast aside because of the successful enema. Here is a pertinent danger. The physican may think that volvulus does not exist. Often, the symptoms of volvulus return, always relieved by enema, but never really cured or permanently controlled. Therefore, even if the enema has been successful, the physician must remain alert and must use proctoscopy or barium enema to establish further maneuvering. Proctoscopy with passage of rectal tube may be necessary to achieve untwisting.

The proved volvulus, now reduced from its acute twisting by enema, barium enema, or protoscopy, is still a danger to the mentally unstable patient, the ignorant, and those patients who have not been properly oriented by the physician.

Phase II. The patient must follow simple rules of correction if volvulus recurs. If the obstruction is easily reduced by the patient, and the attacks are not too frequent, annoying, or frustrating, there is no need for other treatment.

But if on the first examination there is marked distention, tenderness, leukocytosis, fever, tachycardia, malaise, or a combination of these findings suggesting gangrene, one must vary the course.

Proctoscopy must be done now only with extreme caution. If untwisting cannot easily be accomplished, electrolytic and fluid balances are established, and laparotomy must be done as soon as the condition permits. If during the procedure the examiner finds necrosis, mucosal ulceration, or blood, he should discontinue proctosigmoidoscopy immediately because this may induce perforation of the bowel wall. This procedure should also be discontinued if the patient complains of pain. Here, one cannot procrastinate because of emphysema, pulmonary fibrosis, or cardiac involvement, unless the patient is obviously lethally ill and demise is imminent. Betterment of the heart and lung conditions cannot take place until the abdominal distention is relieved, lowering the diaphragm and permitting better respiratory exchange. Clinical common sense and sane courage must exist. Here, the surgeon may "chicken out" and a life will be lost unnecessarily. The decision is difficult, important, and dangerous.

In the elderly patient, prepared as well as one can prepare him, a plan of management follows:

Procedure as Simple as Possible

1. Laparotomy with rapid untwisting in majority of cases.

2. Laparotomy with resection and end-to-end or side-to-side anastomosis, if gangrene is present and the condition permits.

3. Laparotomy with resection of gangrenous tissue and both ends of bowel brought to surface if the condition locally and generally will not permit safe anastomosis.

4. Some prefer the so-called Mikulicz procedure, but we prefer the hasty resection because all gangrenous tissue can thus be removed, fear of gangrenous extension is eradicated, and not much more time is consumed. Reunion of bowel of course is done at a later and safer time.

5. In extremely ill patients, simple cecostomy and colostomy of the closed loop can be done under local anesthesia, save the patient's life, and permit restorative procedures later. Cecostomy alone will decompress the bowel above the volvulus but will not always prevent gangrene if the closed loop remains. Therefore, two simple procedures under local anesthesia are done. First, the cecostomy and if relief seems satisfactory, the left-sided colostomy may not be necessary. Occasionally, the left-sided colostomy must be done hours or days later. This *cannot safely be done,* of course, if the loop is gangrenous.

These rather simple procedures therefore must be selected from the indications mentioned.

Consequently, different measures must be used in the acute volvulus, ranging from enemas, proctoscopy, proctoscopy plus rectal tube (the closed methods of reduction); or if these measures fail or if gangrene is probable, one of the operative procedures mentioned above must be done.

Indications for Therapy in the Interval or Chronic Stage

As stated above, the indications for operation in the acute stage exist only in the instances of gangrene, perforation, or reduction that cannot be readily accomplished by the so-called medical measures.

Therefore, the unresected patients, with successful untwisting medically or the few requiring laparotomy to accomplish the untwisting, form an important group.

Pertinent instructions by the physician must explain the nature of the illness, the control by medical measures, including habitual positioning previously used by the patient, and the appearance or disappearance of abnormal distention. The intelligent patient, having received *proper instructions* from the physician, can safely and often permanently handle his own untwisting successfully with no fear of disaster.

Here, one must impose important "ifs" in the following plan:

I. If attacks recur, successfully controlled by the patient, but the number is great, and intensity of pain, etc., more than passable, this patient then becomes a candidate for the so-called interval resection, which, of course, is much more safely done than when the resection is performed in the acute stage.

II. If the first attack was quite severe and untwisting difficult to achieve by experienced physicians, resection in an interval state is indicated.

III. If the attack occurred in a mentally-ill patient, which is not uncommon, and the mental condition is precariously unstable in the opinion of the surgeon, often with the aid of the internist or psychiatrist, resection is indicated in the early interval state. In this instance, the patient should not be allowed to leave the hospital unless he is accompanied by a professional person, or by a well-informed wife, relative, or nurse who is capable of understanding the situation. If he leaves, it is the physician's duty to warn the family of the danger, their responsibilities in the watchfulness, use of medical measures, and to orient them to return the patient immediately to the hospital in case untwisting is not readily and accurately accomplished. Obviously, the resection in the early interval will abolish this risky period. Our experience indicates that most of these mental patients should be kept in the hospital because twisting often recurs and just as often is unrecognized. The indication for operation is definitely more urgent in the mental patient. In other words, procrastination here can be very dangerous. The mental patient may be euphoric but still dangerously obstructed. His euphoria may fool the best clinician unless the physician realizes that fact.

IV. If, in addition to the volvulus, there exist polyps, single or multiple; diverticula; obstructing bands; or any evidence that some organic lesion accompanies the volvulus, operation is indicated in the interval state without undue delay.

For instance, carcinoma and/or polyps may be situated in a position to cause the volvulus to be more repetitive. Diverticula have been rarely seen in our experience and the literature makes no mention of an increased frequency of diverticula in volvulus. Perhaps volvulus cannot so readily follow if the effects of the infection introduce an induration preventing the looseness required in the formation of the volvulus.

One must bear in mind that volvulus of the cecum may mimic the sigmoid volvulus, and that volvulus of the small bowel may often induce similar symptoms. The cecal and sigmoidal volvulus may coexist. The therapy is easy if the coexistence is recognized by the surgeon. Operation is indicated. Do what is necessary about the sigmoid volvulus according to the indications mentioned above. The cecal volvulus is easily controlled by simple cecostomy after manual operative reduction of the cecal volvulus. The resulting attachment of the cecum to the abdominal wall prevents future cecal volvulus.

Recently, we have encountered volvuli of the transverse and descending colons. In these incidences, medical measures fail to correct and barium enema will demonstrate absence of sigmoid twist, or if present, has been successfully untwisted and demonstrated the true nature of the persistent higher obstruction. In our opinion, volvulus at these two sites is more common than most observers think.

It is this combination of events that poses a problem which has led the professional observer away from the true nature of this condition.

The authors are quite certain that large bowel volvulus, particularly sigmoidal volvulus because of its frequency, has been the contributing cause of some pulmonary and cardiac deaths, and the deaths being attributed to pulmonary or cardiac conditions are recorded under these latter categories.

Actually, the limitation of breathing space by upward pressure of the distended loops upon the diaphragm causes the emphysematous or pulmonary fibrotic patient to experience marked pulmonary dys-

function, hypoxia, atelectasis, and pneumonitis with early death, but at postmortem examination, pathologists may designate the pulmonary-cardiac defect as the culprit and state confidently that paralytic ileus secondary to the chest lesion was also seen. Little does the pathologist realize that if the abdominal distention had been seen early and properly relieved that this death could have been averted. Only when gangrene or perforation occurs does the pathologist indict the sigmoidal volvulus. Consequently, these volvuli are believed to be uncommon and death from them rare. This is true in young patients perhaps, but starting at middle age and increasing as the patient ages, this lesion is more common than the medical profession believes, much more debilitating than the profession thinks, much more dangerous than we believe, and causes a reasonable number of deaths, all not so documented by the pathologist even at postmortem examination.

Our controlled patients are happier and utterly amazed at the absence of the distressing distention which before treatment they accepted as a matter consistent with the aging process from which there was no deliverance!

(The figures and references may be seen in the original article.)

TRANSVERSE MYELITIS ASSOCIATED WITH HEROIN ADDICTION

Ralph W. Richter, MD, and Roger N. Rosenberg, MD,
JAMA 206(6):1255–1257, Nov 4, 1968.

Acute transverse myelitis involving thoracic segments was observed as a new complication of heroin addiction in four Negro men. Three of the four patients had not taken heroin for periods of one to six months either while in prison or the hospital. The acute myelitis developed shortly after heroin was taken again intravenously. At onset, three patients suddenly became paraplegic, and moderate paraparesis developed in one. All four demonstrated thoracic sensory levels. Myelograms were normal for the three patients on whom they were performed. One patient died five weeks after taking heroin again. Extensive necrosis of the spinal cord in the lower thoracic region was found at necropsy. Another patient died, but no autopsy was performed. Mild paraparesis with sensory loss remains in one man, and severe paraparesis with sensory loss persists in the other survivor.

Numerous medical complications have been reported in addicts who self-administer heroin under unsterile conditions. These include skin abscesses and ulcerations, thrombophlebitis, pulmonary infections and infarcts, bacterial and fungal endocarditis, hepatitis, septicemia, and tetanus. Acute pulmonary edema and other fatal reactions are also common. The New York City Medical Examiner reported 1,586 deaths from acute narcotism from 1950 to 1961. The yearly number of such deaths has recently increased. During 1967 there were 670 deaths from acute narcotism.

Harlem Hospital is a 1,000-bed municipal facility serving 300,000 citizens of central Harlem. Many medical complications of heroin addiction are treated there. During March 1968, 29 (9 percent) of 318 patients discharged from the Medical Department were heroin addicts. The Neurological Service has also treated complications in addicts, such as septic cerebral artery emboli and cerebral arterial thromboses, status epilepticus, bacterial and tuberculous meningitis, injection neuropathies, polyneuritis, and acute massive myoglobinuria. The purpose of this communication is to present four cases which illustrate the recently observed findings of acute transverse myelitis associated with heroin addiction.

Report of Cases

Case 1.—A 33-year-old Negro man had taken five to seven "bags" of heroin intravenously each day over a 12-year period. In October 1964 he was sentenced to Rikers Island Prison. After his release in late January 1965, he began using heroin again. On Feb 10 he injected two bags of heroin intravenously and then fell asleep. He awoke three hours

From the Neurology Department, Columbia University College of Physicians and Surgeons and the Neurology Service, Department of Medicine, Harlem Hospital Center, New York.
Reprint requests to Neurology Service, Harlem Hospital Center, 136th St and Lenox Ave, New York 10037 (Dr. Richter).

later with numbness and paralysis of both legs. The following morning he was taken by ambulance to Harlem Hospital. There was a flaccid paralysis of both lower extremities. Deep tendon reflexes were present in both legs, and the plantar responses were normal. Pain and temperature appreciation was lost below the T-5 level. Vibration sense and position sense were minimally diminished distally in both legs. He had acute urinary retention necessitating an indwelling catheter. The spinal fluid was under a pressure of 110 mm H_2O with normal manometrics. The fluid contained eight lymphocytes per cubic millimeter, a protein level of 38 mg/100 ml, results of serological study were normal. Seven days after onset of symptoms, he signed out of the hospital against medical advice. He then had moderate weakness of both legs with sensory deficits and still required a catheter. A cystometrogram in June 1965 demonstrated a hypertonic neurogenic bladder. His neurologic sequelae persisted. Examination in March 1968 showed a mild weakness of both legs. The knee and ankle jerks were hyperactive, and the plantar responses were extensor in type. Pain and temperature appreciation were mildly reduced between the T-5 and T-4 levels, and there was minimal reduction in vibration and position sense distally in both legs. He still requires an indwelling urinary catheter.

Case 2.—A 31-year-old Negro man had taken two to four bags of heroin intravenously each day when possible from 1953 to 1962. During this time he served three prison sentences and was voluntarily hospitalized once. He was released from a six-month incarceration two months prior to onset of symptoms. On March 30, 1962, he experienced several episodes of numbness and weakness of both legs, which lasted a few minutes following heroin injection. On April 7 he injected one pack of heroin intravenously and fell asleep. He awoke with complete paralysis and numbness of both legs and loss of bladder sensation. He was admitted to Harlem Hospital. There was a flaccid paralysis of both legs. Deep tendon reflexes were absent in both legs, and plantar responses were normal. Pain, light touch, and temperature appreciation were markedly diminished below the T-5 level. The spinal fluid contained no cells; protein level was 41 mg/100 ml; and results of serological study were normal. A myelogram was normal. He was treated at the Rehabilitation Service of the Montefiore Hospital and during a seven-month period showed only slight improvement. Neurologic examination in January 1968 demonstrated severe weakness of both legs. The left leg was more severely involved, and he could stand briefly only by supporting himself on the right leg. Atrophy of proximal and distal muscles of both legs was present. Tone was markedly increased in both legs, and frequent extensor spasms were observed. Clonus of both knee jerks was present. Ankle jerks could not be tested because of bilateral drop foot with Achilles tendon contractures. The plantar responses were extensor in type. Pain and temperature appreciation was markedly reduced below the T-5 level on the right side more than on the left. Vibration and position sense were absent in the left foot and reduced in the right foot. A neurogenic bladder was present and periodic rectal incontinence was experienced.

Case 3.—A 33-year-old Negro man was addicted to heroin from 1948 to January 1965 and had taken between three to five bags intravenously each day. During 1957 he was voluntarily admitted to the Federal Narcotics Hospital in Lexington, Ky, for six months. Immediately after leaving the hospital, he began taking heroin again, and several weeks later rapid onset of weakness and numbness of both legs developed. He improved slightly but continued to need a cane to assist ambulation. In October 1965 he was evaluated at Harlem Hospital. Moderate weakness and diffuse muscle wasting of both legs were present. Hyperactive knee jerks, sustained ankle clonus, and extensor plantar responses were observed. Position sense and vibratory appreciation were normal, but pin-prick, light touch, and temperature appreciation were diminished below the T-4 level. The spinal fluid contained no cells; there was a protein level of 26 mg/100 ml; and findings of serological study were normal. X-ray films of the spine and a myelogram were normal. The neurologic findings were unchanged at his last clinic visit on Aug 1, 1967. On Sept 10 his mother found him dead in bed. The spinal cord was not removed by the Medical Examiner.

Case 4.—A 30-year-old Negro man had taken four to six bags of heroin intravenously each day when possible for 13 years. In August 1965 he was sentenced to Riker's Island Prison and was released Oct 10. He immediately took heroin again. On Oct 15 he injected a bag of heroin intravenously and fell asleep in a hallway. He awoke three to four hours later and was unable to move his legs. He was taken by ambulance to Harlem Hospital. There was a flaccid paralysis of both lower extremities.

Deep tendon reflexes were absent in both legs, and the plantar responses could not be obtained. All sensory appreciation was lost below the T-8 level. Acute urinary retention was present and an indwelling catheter was required. The spinal fluid was under a pressure of 205 mm H_2O and manometrics were normal. The fluid contained eight lymphocytes per cubic millimeter, a protein level of 66 mg/100 ml, and γ-globulin was 14 percent of the total protein (normal, up to 15 percent). A myelogram was normal. He was treated with 4 mg of dexamethasone (Decadron) every six hours initially. By Oct 19 he showed flicker movements of his toes. He then complained of severe pains and burning sensations in both legs. The motor and sensory findings remained unchanged. On Nov 15 he suddenly became comatose, generalized seizures developed, and he had a period of cardiac arrest of undetermined duration. Following external cardiac massage, his breathing was controlled by a positive pressure respirator. He remained comatose and died on Nov 22.

At necropsy, massive emboli in the pulmonary artery bilaterally were found by the Medical Examiner. The entire spinal cord was examined. At the level of T9-11, the transverse diameter of the cord was decreased by an indentation. This region was softer than the superior and inferior segments of the cord. Sections of the spinal cord at the T-10 level showed a large necrotic area involving all the gray matter plus most of the ventral portions of the posterior columns. None of the anterior horn cells remained. Rarefaction of white matter was seen around the central zone of necrosis. A zone of pallor was seen in the lateral columns. In the central zone of necrosis, only a few remnants of myelin sheaths could be found. Tissue spaces were widened. The necrotic tissue was replaced by large, lipid-laden phagocytes. Vessels in the zone of necrosis showed endothelial hyperplasia. The anterior spinal artery lumen was not occluded. No evidence of arteritis was evident.

Comment

Heroin addiction is a major public-health problem throughout New York City. The Health Department registry lists between 35,000 to 40,000 known addicts, and twice this number may now actually reside within the city. In Harlem it is estimated that 50,000 addicts are daily moving in and out to obtain their heroin supply. Heroin has already been "cut" some six to seven times when it reaches the "pusher." Quinine, lactose (benita) and mannitol are then added to further cut the heroin. Diluted heroin is currently sold in $2 and $5 packets or bags. The smaller packet may contain as little as 0.004 of an ounce of pure heroin or a possible morphine equivalent of 5 to 8 mg. The larger packet may contain an equivalent of 15 to 30 mg of morphine. The user has no way of knowing the strength of the material he injects except by the kick he receives. The addicts in our series injected between two to seven bags of dissolved heroin intravenously each day when available, or a possible dosage equivalent of morphine varying from 20 mg to 200 mg. True allergic reactions in the form of rash, urticaria, angioneurotic edema, or anaphylaxis may follow heroin administration. Heroin may depress central vasomotor control and result in diminished vasoconstrictor activity and a decrease in response to circulatory reflexes regulating blood pressure. The release of histamine after heroin administration may also contribute to a severe hypotensive reaction. Quinine was probably introduced as an adulterant for cutting heroin in order to prevent the occurrence of malaria in the addict. Quinine has also been found to potentiate the analgesic effects of narcotics. When given intravenously or in high doses by other routes, quinine may cause a severe hypotensive reaction by direct depression of myocardium and peripheral vasodilatation. Acute blindness has rarely been caused by large doses of quinine.

Transverse myelitis has been described in association with many etiologic factors. Infectious diseases, demyelinating processes, neoplasms, and metabolic disturbances have all been implicated. Acute vascular or ischemic lesions of the spinal cord may cause these symptoms. Spinal artery embolism is probably an uncommon cause. Toxic reactions to drugs, such as arsenicals and sulfonamides, and reactions to contrast media have also been recorded. Myelitis has followed smallpox or rabies vaccination. Other allergic or auto-immune predisposing factors have also been suggested.

The history and follow-up of these cases was not consistent with a demyelinating disease process, such as multiple sclerosis. No other medical illnesses could be implicated by extensive medical work-up. Compressive spinal-cord lesions were ruled out by manometric studies of the spinal fluid and myelography. Myelitis developed in three of the four patients shortly after they returned to intravenous use of heroin after release from the hospital or prison. The acute onset of paralysis and sensory loss occurred within several hours after an intra-

venous injection of heroin. These factors suggest an allergic or hypersensitive reaction.

The thoracic spinal cord was involved in all of our cases. Postmortem examination of patient 4 revealed a large necrotic lesion in the spinal cord at the T9-11 level. There were no recognizable occlusions or emboli in the spinal-artery circulation. A temporary vascular lesion could not be ruled out, since the thoracic spinal cord has a relatively insufficient blood supply. We can only speculate as to what produced the thoracic lesions in our patients. It is possible that a severe systemic reaction to the heroin, quinine, or other adulterants led to a temporary vascular insufficiency in the vulnerable thoracic-cord circulation. Hypersensitivity reactions or even direct toxic effect of the drugs should also be considered. Further studies are needed to clarify this problem.

Two additional cases of acute thoracic myelopathy in heroin addicts have been studied. Their history and findings were identical to those mentioned earlier. One has almost completely recovered and the other patient still has moderate spastic weakness of both legs and sensory changes below the T-8 level.

Michael Lyons, MD, and Fernando P. Aleu, MD, of the New York City Medical Examiner's office, performed the autopsy and prepared the spinal cord sections in case 4. Angeline R. Mastri, MD, reviewed the microscopic sections and Edward Entin prepared the photomicrographs. James E. Wesley, MD, assisted with case 4. Albert D. Anderson, MD, brought case 2 to our attention and made the past records available.

Generic and Trade Names of Drugs

Dexamethasone—*Decaderm, Decadron, Deronil, Dexameth, Gammacorten, Hexadrol, Maxidex.*
Mannitol—*Osmitrol.*

(The figures and references may be seen in the original article.)

INTRAOCULAR TREPONEMES

Ernest H. Christman, MD; Robert W. Hamilton, MD; Charles L. Heaton, MD; and Iris M. Hoffmeyer, MD, Philadelphia, Arch Ophthal 80(3):303–307, Sept 1968.

Using the Fluorescent Antibody Darkfield (FADF) method, the aqueous humor of 36 patients was examined for treponemes. Each patient had one or more of the following conditions: chronic uveitis, chorioretinitis, interstitial keratitis, dislocated lenses, optic atrophy, or neurosyphilis. Treatment with ampicillin and probenecid was instituted in seven of 12 patients whose aqueous humor contained organisms resembling *Treponema pallidum.* The most significant response to treatment was seen among six patients with active uveitis. Five of these patients had initial resolution of uveitis with disappearance of intraocular treponemes. Two of these five patients subsequently developed recurrent uveitis concomitant with reappearance of intraocular treponemes. One patient had persistent uveitis and intraocular treponemes despite therapy.

A recent report by Smith and Israel indicated that organisms resembling *Treponema pallidum,* which stain with specific fluorescein-conjugated antibody, may be found in the aqueous humor and cerebrospinal fluid of patients with syphilitic chorioretinitis, chronic uveitis, and neurosyphilis. Similar findings have been reported by Goldman and Girard in two cases of congenital syphilis with interstitial keratitis and deafness. Goldman and Girard have further reported that interstitial keratitis and uveitis improved in patients treated with ampicillin and probenecid. This report summarizes our experience using the Fluorescent Antibody Darkfield (FADF) technique to demonstrate intraocular treponemes in patients with chronic inflammatory eye disease and presents our observations on the response of these patients to treatment with ampicillin (Omnipen) and probenecid.

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From the Departments of Ophthalmology and Dermatology, University of Pennsylvania Division of the Philadelphia General Hospital and the Venereal Disease Control Section, Division of Epidemiology, Community Health Services, Philadelphia Department of Public Health.

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Reprint requests to Duhring Laboratories, Department of Dermatology, Hospital of the University of Pennsylvania, 3400 Spruce St, Philadelphia 19104 (Dr. Heaton).

Materials and Methods

The 36 patients in this study were seen in the Philadelphia General Hospital Eye Clinic for interstitial keratitis, chronic uveitis, dislocated lenses, chorioretinitis, optic atrophy, and neurosyphilis. Each patient was questioned specifically regarding a past history of syphilis and was examined for signs of late syphilis. Venereal Disease Research Laboratory (VDRL) and Fluorescent Treponemal Antibody-Absorption (FTA-ABS) tests were performed on each patient's serum.

The aqueous humor was collected by anterior chamber paracentesis as described by Goldman and Girard. Each specimen was prepared for fluorescence microscopy in the following manner: The 0.1 ml specimen was injected into two capillary tubes and was frozen at −20 C to −40 C until the FADF test was performed. The FADF technique employed was a modification of the direct method fluorescent technique described by Yobs et al. After thawing, the specimen was expelled onto a clean pre-etched microscope slide and air dried. The material was fixed by flooding the slide with freshly prepared 3 percent formaldehyde solution for two minutes. It was then washed, dried, and covered with a minimal amount of normal human serum. Fluorescein-conjugated human specific anti-*Treponema pallidum* antibody globulin was added to this, and the specimen was incubated at 35 C to 40 C for two minutes or until dry. The slide was then rinsed with distilled water for five seconds, counterstained with 1 percent Evans blue for ten minutes, soaked in pH 7.2 phosphate buffered saline, and was mounted with pH 9.0 mounting fluid and cover slip. The specimen was then examined for fluorescein-stained treponemal forms using a microscope (Leitz Labolux III A) with the following filter combination: exciting filter (Leitz BG 12) and barrier filter (Leitz OG1).

The human fluorescein-conjugated anti-*Treponema pallidum* antibody globulin used in this study has been prepared by absorption with *Treponema reiteri* to remove nonspecific cross-reacting antitreponemal antibodies. However, this fluorescent antibody will not distinguish *Treponema pallidum* from *Treponema pertenue, Treponema carateum* and *Treponema cuniculi.* The specificity of the conjugate was not further evaluated by us. As a positive control, a suspension of lyophilized *T pallidum,* Nichols strain (FTA-ABS test antigen), was examined using the FADF method. Treponemes were reported as being

Patients With Intraocular Treponemes

Case	Ocular Findings	Venereal Disease History	Serology		Completed Ampicillin Therapy
			VDRL	FTA-ABS	
1	Argyll Robertson pupils	General paresis—1954, treatment PAM* 1.2 million units daily for 14 days	4 dilutions	R† (1-2+)	No
2	Interstitial keratitis, uveitis, chorioretinitis	Syphilis denied	NR‡	NR	Yes
3	Uveitis, chorioretinitis	Primary syphilis—1936, treatment; 20 arsenical injections, 40 bismuth injections; retreated—1944, agent unknown	WR§	NR	Yes
4	Anterior uveitis	Syphilis denied	NR	NR	Yes
5	Chorioretinitis, optic atrophy	Late congenital syphilis—1946, treated with penicillin	2 dilutions	R (2-3+)	No
6	Uveitis, chorioretinitis	Exposed to syphillis at age 14, never diagnosed or treated	NR	NR	Yes
7	Interstitial keratitis, uveitis, chorioretinitis, dislocated lenses, optic atrophy	Syphilis denied	NR	NR	Yes
8	Uveitis	Syphilis denied	WR	NR	Yes
9	Light-near dissociation of pupillary reflex	Syphilis denied, gonorrhea—1960	WR	NR	No
10	Interstitial keratitis, anterior uveitis	Latent syphilis—1963, untreated; primary syphillis—1966, bicillin 2.4 million units; secondary syphilis—1967, bicillin 2.4 million units	8 dilutions	Not done	No
11	Optic atrophy	Syphilis denied	1 dilution	R (1-2+)	Yes
12	Chorioretinitis, uveitis	Latent syphilis—1945, treated with penicillin	WR	R (1-2+)	No

* PAM = Penicillin aluminum monostearate.
† R = Reactive.
‡ NR = Nonreactive.
§ WR = Weakly reactive.

present in the patient's aqueous humor only when the organisms showed characteristic morphology and a fluorescence greater than that of the positive control. As a negative control, the aqueous humor obtained at cataract surgery from three patients was examined. Each negative control patient's serum was nonreactive to VDRL and FTA-ABS tests. Treponemes were not found in these negative control specimens.

Those patients whose aqueous humor contained treponemes were treated with ampicillin 1.5 grams and probenecid 0.5 grams orally, four times daily for ten days. The first post-treatment anterior chamber paracentesis was performed from two to six weeks after the completion of therapy. Subsequent paracenteses were performed at approximately monthly intervals.

Results

The clinical features of the 12 patients whose aqueous humor contained treponemes are summarized in the Table. Seven of the 12 patients were treated with the ampicillin-probenecid regimen and observed for periods greater than two months. Five patients did not return for further study or treatment. There were six cases of active uveitis and one case of optic atrophy among the treated patients. Three of the six cases of uveitis improved clinically after therapy, and their follow-up aqueous humor examinations did not reveal treponemes during six months of post-treatment observation. Two cases (3 and 6) improved clinically while taking ampicillin and probenecid but developed recurrent uveitis two and four months after completion of therapy. Moreover, at the time of recurrence, aqueous humor taken from these two patients contained treponemes. Following therapy one case (4) continued to have active anterior uveitis, as well as persistent treponemes in the aqueous humor. Although there was no clinical improvement in the vision of the patient with optic atrophy, treponemes were not found in the post-treatment aqueous humor.

Report of Cases

Case 1.—A 67-year-old Negro woman was admitted to the hospital in February 1954 with a six-month history of inability to concentrate. On physical examination she was confused and had a loss of recent memory. Her pupils did not react to light but did react to accommodation. Slight pallor of the optic discs was noted. Deep tendon reflexes were symmetrical and hypoactive. Her coordination appeared normal; Romberg's sign was absent. The serum Kahn test was reactive at 1,024 dilutions. The cerebrospinal fluid (CSF) contained 110 cells/cu mm, 79 percent lymphocytes; the protein was 93 mg/100 ml; the Kahn test was reactive at 256 dilutions, and the colloidal gold reaction was 5555432100. A diagnosis of general paresis was made, and the patient received a total of 16.8 million units of penicillin aluminum monostearate (penicillin procaine suspension with aluminum stearate) over 14 days. When seen in the Eye Clinic in 1967, the patient's ocular examination revealed only Argyll Robertson pupils. Her VDRL was reactive at 4 dilutions, and her FTA-ABS was reactive. The aqueous humor obtained from the right anterior chamber contained treponemes. The patient did not return to clinic for follow-up.

Case 2.—This 36-year-old Negro woman came to the Eye Clinic in June 1967 because of pain in the right eye following a recent injury. She gave a history of poor vision since age 5. Although she denied a past history of syphilis, congenital syphilis could not be excluded, since her parents and siblings were not available for examination. Visual acuity in each eye was limited to counting fingers. There was right exotropia, bilateral interstitial keratitis with chorioretinitis, and an active uveitis with cells and flare in the left eye. Her VDRL and FTA-ABS tests were nonreactive. The aqueous humor obtained from the right anterior chamber contained treponemes, and the patient was treated with ampicillin and probenecid. One month following treatment, visual acuity in the left eye improved to 20/40 and there was clearing of cells and flare. The left eye remained free of inflammation for a follow-up period of seven months. Visual acuity in the right eye was unchanged. No treponemes were found in the aqueous humor three and seven months after treatment.

Case 3.—This 53-year-old Negro man had primary syphilis in 1936. He was treated with 20 bismuth injections followed by 20 arsenical injections and an additional 20 injections of bismuth. In 1937, he was admitted to the hospital because of headaches, weakness in his left arm and leg, and blurred vision of five-day duration. His neurologic examination was, however, normal. The Kahn test was reactive 4+ and the cholesterol antigen test was reactive 4+. Study of the patient's CSF revealed one white blood cell per cubic millimeter, a negative Wassermann

and a negative cholesterol antigen test. The patient was retreated in 1944 in the Philadelphia City Health Clinics.

In June 1963 he was admitted to the hospital because of poor vision. On visual acuity testing, he could barely distinguish fingers. There were keratitic precipitates with corneal haze in both eyes and posterior synechiae in the right eye. The VDRL, Kolmer, and Reiter Protein Complement Fixation tests performed on his serum were all nonreactive. Following treatment with local antibiotics, local and systemic corticosteroids, atropine, and phenylephrine, his visual acuity improved to 20/100 in each eye. Since 1963 he has been observed in the Eye Clinic for chronic recurrent anterior uveitis of both eyes.

In September 1967 his visual acuity was 20/40 in each eye. Active anterior uveitis with old pigmented keratitic precipitates and posterior synechiae was seen on slit-lamp examination. Funduscopic examination revealed peripheral scarring of both fundi, compatible with old inactive pars planitis. Neurologic examination was normal. The VDRL was weakly reactive; the Kolmer and FTA-ABS were nonreactive. Study of the patient's CSF revealed no cells, a protein of 19 mg/100 ml, and a nonreactive VDRL. Treponemes were demonstrated in the aqueous humor of the patient's right eye. Treatment consisted of ampicillin, probenecid, and topical corticosteroids. One month after the completion of therapy, there was a reduction in the cells and flare in the anterior chamber. At that time treponemes were not found in the aqueous humor. Two months following therapy the patient was noted to have a slight flare in both eyes. Treponemes were again found in the aqueous humor. During the next month, remission of the anterior uveitis occurred without treatment. Four months following therapy, there was no evidence of active anterior uveitis, and terponemes were not found in the aqueous humor.

Case 4.—This 25-year-old Negro woman, who denied a history of syphilis, suddenly developed total deafness in June 1966. In September 1966 neurologic examination revealed a right peripheral facial palsy, bilateral nerve deafness, primary horizontal nystagmus on left lateral gaze, and a right Babinski's reflex. An Unheated Serum Reagin test was nonreactive. Examination of the CSF revealed 4 red blood cells per cubic millimeter, a protein of 20 mg/100 ml, a nonreactive Kolmer test, and a colloidal gold reaction of 2221100000. Viral studies were negative. In November 1967 the patient experienced pain in her left eye. She was found to have an anterior uveitis in the left eye with 3+ cells and flare. There was no anterior uveitis in the right eye. Funduscopic examination of both eyes was normal; visual acuity was 20/15 in the right eye and 20/25 in the left eye. The VDRL and the FTA-ABS tests were nonreactive. The CSF contained no cells; the protein was 25 mg/100 ml, and the VDRL test on the spinal fluid was nonreactive. In January 1968 treponemes were demonstrated in the aqueous humor of the patient's left eye. Two months following treatment with ampicillin and probenecid, the patient had persistent anterior uveitis and intraocular treponemes.

Case 5.—This 40-year-old white man was found to have rhagades and a reactive Hinton test in 1946. A diagnosis of late congenital syphilis was made at that time. In 1947, results of the patient's neurologic examination were normal, but sluggish pupillary light reflexes, iris pigment on the right lens, and pallor of the right optic disc were noted. The Hinton test was still reactive, and the Kahn test was reactive at 122 dilutions. The patient claimed that during the years between 1946 and 1967 he had received 80 injections of penicillin. It was not possible to confirm this. In 1967, there were no abnormal neurologic findings. Optic atrophy was present in the right eye. An old patchy chorioretinitis with bone corpuscular clumping of pigment was present in both eyes. The VDRL test was reactive at 2 dilutions; the FTS-ABS test was reactive. Treponemes were found in the aqueous humor of the right eye. The patient did not return for therapy.

Comment

In this study, treponemes which stain with specific fluorescein-conjugated antitreponemal antibody have been found in the aqueous humor of patients with chronic uveitis, chorioretinitis, interstitial keratitis, dislocated lenses, optic atrophy, and neurosyphilis. Smith and Israel and Goldman and Girard have made similar observations. Using ordinary darkfield microscopy, both groups have shown that these organisms have motility that is characteristic of *T pallidum*. Smith and Israel have inoculated these organisms into experimental animals. Aqueous humor taken from a patient with chorioretinitis was inoculated into the testis of a rabbit, and a darkfield-positive orchitis was produced. Cerebrospinal fluid taken from a tabetic patient was inoculated intradermally into a squirrel monkey. Subsequently, treponemes were observed in the animal's aqueous humor, and a darkfield-positive lesion appeared on

its nares. In addition to intraocular treponemes which stain with fluorescein-conjugated antibody, Goldman and Girard have reported the occurrence of intraocular treponemes which do not stain with fluorescent antibody. The exact significance of these organisms is unknown.

On the assumption that these treponemal forms are indeed *T pallidum,* it was decided to treat the patients in this study with antibiotics. Orally administered ampicillin and probenecid were chosen on the basis of the following studies. Kurose et al have demonstrated that a significant aqueous humor level of ampicillin is attained after oral administration. This level exceeded that required for in vitro immobilization of *T pallidum*. Goldman has shown that levels of ampicillin in the aqueous humor may be enhanced by concomitant administration of probenecid.

The interstitial keratitis, chorioretinitis, and optic atrophy seen in cases 2, 3, 6, 7, 8 and 11 appeared unchanged following treatment with ampicillin and probenecid. Since these conditions represent the result of previous inflammation, no clinical improvement would be expected. In active uveitis, where active inflammation was present, clinical improvement was seen (cases 2, 3, 6, 7, 8). The recurrence of uveitis in two of these cases (3 and 6) correlated with the reappearance of treponemes in the aqueous humor. While the presence of these organisms was associated with disease activity, their pathogenicity has not been demonstrated.

The serologic findings in the cases reported here differ from those of other investigators. The FTA-ABS test was nonreactive in seven of the 11 patients whose serum was examined. From the work of Deacon et al it would be expected that 94.9 percent of the patients with late central nervous system, congenital, and cardiovascular syphilis would have reactive FTA-ABS tests. Because the nonreactive FTA-ABS tests were questioned, split specimens were examined by our laboratory and the Venereal Disease Research Laboratory in four cases (4, 6, 7, 8). The nonreactive FTA-ABS tests were confirmed. While Smith et al have emphasized the value of the FTA-ABS in confirming the diagnosis of seronegative ocular and neurosyphilis, they do describe two cases of presumed ocular syphilis in which the FTA-ABS tests were nonreactive. Similarly, Goldman and Girard described a case in which intraocular treponemes were found in FADF examination but the FTA-ABS test was nonreactive.

The persistence of these treponemal forms in the aqueous humor after penicillin G therapy has been described by others. While this may be explained by the poor ocular penetration of penicillin G, the possibility of reinfection of the patient cannot be eliminated. Collart, who demonstrated persistence of treponemes after treatment in man and experimental animals, has suggested that the interval between infection and treatment may be important in determining persistence.

This report has documented that intraocular treponemes resembling *T pallidum* may be found in the aqueous humor of patients with chronic uveitis, interstitial keratitis, dislocated lenses, optic atrophy, and neurosyphilis. A correlation was found between the activity of the eye disease and the presence of treponemes. The initial response of patients with active uveitis to treatment with ampicillin and probenecid was encouraging. The significance of these findings and their therapeutic implications must come from further investigation into the nature of these treponemal forms and of the distribution of antibiotics in the eye and central nervous system.

Mrs. Thelma Meade performed FADF examinations of the aqueous humor under the supervision of Mr. James R. Copeland, Director, Public Health Laboratories, Philadelphia Department of Public Health.

Fluorescein-conjugated antitreponemal antibody was supplied by Douglas S. Kellogg, Jr., PhD, Venereal Disease Research Laboratory, National Communicable Disease Center, Atlanta, Ga.

Ampicillin used in this study was supplied as Omnipen by John Silverio, MD, of Wyeth Laboratories, Philadelphia, Pa.

Key words.—Ampicillin; FADF; fluorescent antibody darkfield; syphilis; *Treponema pallidum,* intraocular; uveitis.

Generic and Trade Names of Drugs

Ampicillin—*Omnipen, Penbritin, Polycillin, Principen.*
Probenecid—*Benemid.*
Phenylephrine—*Neosynephrine.*

(The references may be seen in the original article.)

SNAKEBITE IN THE TROPICS

H. Alistair Reid, OBE MD FRCPE FRACP DTM&H,*
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Medically important snakes have fangs at the front of their mouths which enable them to inject venom efficiently. These are the "poisonous" snakes and there are three types—elapids (neurotoxic), seasnakes (myotoxic), and vipers (vasculotoxic). The elapid family have short fixed fangs (covered by a gum-fold, the vagina dentis); they include cobras, mambas, kraits, coral-snakes, and all the Australian poisonous snakes such as taipans and tiger snakes. Seasnakes have very short fixed fangs and characteristic flat, rudderlike tails; they are common in Asian coastal waters. Vipers have long, erectile fangs, triangular heads, and, usually, short fat bodies. Vipers are subdivided into crotaline or pit vipers, having a thermosensitive pit between eye and nose, and viperine vipers, without pits. The pit detects warm-blooded prey in the dark. The "non-poisonous" snakes are also of three types—small burrowing snakes often resembling worms, large constricting snakes such as pythons or boas, and the numerous family of colubrine snakes. Some colubrines have fangs at the back of the mouth, but, though technically venomous, their bites are harmless to man, with the rare exception of some back-fanged snakes in Africa such as the boomslang.

The distinction of poisonous from non-poisonous snakes is often difficult, but is *not* usually important for the clinician; he should be able to diagnose whether or not a patient has poisoning, and, if so, of what type and severity.

Epidemiological studies have confirmed that snakebite in the tropics is a rural and an occupational hazard. Most bites occur in daylight and on the foot or ankle because the victim treads on or near the snake. The severity of poisoning is not related to the time of the bite, breeding habits of the snakes, or the age of the victim.

Incidence of Poisoning

About 15 drops of viper venom could be fatal to an adult man; 3 drops of cobra venom could be lethal; and one drop of seasnake venom could kill 5 men. Fortunately, however, biting human beings is a defensive reaction which rarely results in much venom being injected. The paramount fact about bites of man by poisonous snakes is that more than one-half of the victims will have minimal or no poisoning. Only about one-quarter will develop systemic poisoning. Hence poisonous snakebite is not synonymous with snakebite poisoning.

Fear and Emotional Reactions

The most common symptom following snakebite (whether the snake is poisonous or non-poisonous, and, if poisonous, regardless of the venom injected) is fright—particularly the fear of rapid and unpleasant death. Fear in varying degrees is present in all victims bitten by snakes and often dominates the clinical picture. Emotional symptoms come on rapidly, within minutes of the bite, whereas symptoms of systemic poisoning rarely appear until a half to one hour after the bite. The frightened patient may appear semiconscious, with cold, clammy skin, feeble pulse, and rapid shallow breathing. These symptoms resolve dramatically after a placebo injection.

Many doctors become emotionally affected by having to deal with snakebite patients because they are unfamiliar with the problem. Even in the tropics, where snakebite is comparatively common, cases often receive unwarranted prominence in the local press.

Diagnosis

Local swelling starts within a few minutes of a viper bite if venom is injected. It is a valuable clinical sign, because if swelling is absent and one knows the biting snake was a viper then poisoning can be immediately excluded. Local swelling is also a feature of poisoning by Asian cobra bites, though it may not appear for one to two hours (African cobra bites are not sufficiently documented to indicate whether local swelling is a reliable feature). Other elapids (such as mambas and kraits) and the seasnakes have no local effects. Local pain in snakebite is extremely variable and of no help in diagnosis.

The important early diagnostic signs of systemic poisoning are as follows: Viper—blood-stained spit; later, nonclotting blood. Elapid—ptosis; glossopharyngeal palsy. Seasnake—general myalgia; three to five hours later, myoglobinuria.

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* Senior Lecturer and Honorary Consultant Physician, Liverpool School of Tropical Medicine.

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Nonclotting blood is best detected using a capillary tube with blood taken from a finger prick. The tube should be kept horizontal at room temperature for 20-30 minutes and then raised vertically. Nonclotting blood runs out of its own accord. Myoglobinuria shows as a brown or red colour of the urine (seasnake bite poisoning does not cause haemoglobinuria).

Usually, the minority of victims who receive a venom dose large enough to cause systemic poisoning will already have signs of this by the time they see a doctor. In the rare cases seen soon after the bite, within the latent period between bite and possible onset of systemic symptoms (1-2 hours generally but up to 10 hours with some elapids), the patient should be given a placebo injection and then carefully observed every half hour by the doctor for these early systemic signs.

There are exceptions to the above generalizations. The South American rattlesnake has neurotoxic, not haemorrhagic, effects although it is a pit viper. Some Australian elapid snakes have vasculotoxic and coagulation effects although they are principally neurotoxic. Some vipers (such as the puff adder and the gaboon viper in Africa) do not affect clotting.

Diagnosis of Severity

Viperine poisoning is severe if within one to two hours of the bite swelling is above the knee or elbow, shock is evident, or haemorrhagic signs besides haemoptysis develop (gum bleeding, ecchymoses, positive tourniquet test, and so on do not usually appear for four to five hours).

Elapid poisoning is severe if neurotoxic signs start within one hour or less of the bite and rapidly progress to respiratory failure. Mental confusion strongly suggests respiratory failure, though ptosis and glosso-pharyngeal palsy can make assessment of mental awareness difficult. Shock may also be a feature of severe elapid poisoning.

Severe seasnake poisoning is shown by myoglobinuria as early as one to two hours after the bite, and by the development within a few hours of respiratory failure.

Later Effects

Blisters around the site of the bite are common in cobra and viper envenoming. Blisters extending up the limb in viper bites suggest a large dose of venom; they may be serous or sanguineous. Local necrosis is characteristic of poisoning from Asian cobra bites and some viper bites (such as the African puff adder). Necrosis can be extensive but it is usually superficial; involvement of tendons, muscle, and bones is exceptional. Bacterial infection follows necrosis and may spread to joints. But in the absence of necrosis or meddlesome local measures such as incision, application of dressings, and so on bacterial infection virtually never occurs.

Even without specific treatment the mortality in snakebite is low. Generally speaking deaths are most rapid after elapid bites, especially cobra bites (average death time is about five hours after the bite), and most protracted after viper bites (average is two to three days after the bite). Death in seasnake bite (usually 12 to 24 hours after the bite) and in elapid bite is mainly due to respiratory failure; shock and haemorrhage into vital organs are the main causes of death in viper bites.

In the absence of necrosis, pain after viper bites rarely exceeds two weeks. Swelling usually resolves completely in two to three weeks, rarely in two to three months, and in exceptional cases the limb may remain permanently swollen. If blisters are left alone and no dressing is applied they rupture spontaneously about two weeks after the bite and dry up in an additional one or two weeks. If dressings are applied infection usually follows and greatly prolongs healing. Healing of local necrotic lesions varies according to the extent of the lesions and the treatment given, but requires at least a month, and may take from five to six months or longer even with expert surgical attention. In patients who recover without receiving specific antivenom, systemic symptoms generally subside quickly. Neurotoxic features of elapid systemic poisoning resolve in two to three days as a rule, but exceptionally may persist as long as two weeks. However, the myotoxic effects of systemic poisoning from seasnake bite are prolonged and full recovery may take several months. The transaminases are a sensitive laboratory guide to the muscle damage. In systemic viper bite poisoning shock and haemorrhagic features generally resolve within a week, but in bites by some vipers coagulation changes may persist for two to three weeks or even longer.

First-aid Treatment

First-aid comprises the measures taken by the victim or associates before receiving medical treatment. Recommendations (it will be rare indeed for the doctor to have to apply them personally) should be short, simple, practicable, and more helpful than harmful. Reassurance is most important, as the

danger of snakebite is greatly exaggerated. The site of the bite should be wiped and covered with a handkerchief or cloth; it should not be incised, as this frequently introduces infection. A firm but not tight ligature should be applied just above the bite, using cloth, handkerchief, or grass. The victim should then go to the nearest hospital. If available, aspirin or alcohol in moderation is helpful. If the snake has been killed it should be taken to hospital; otherwise it should be left alone, since attempts to find or kill it often result in further bites.

These recommendations are generally applicable to the tropics, but in special circumstances (for example, in the case of a sophisticated expedition) modifications may be appropriate.

Medical Treatment

Reassurance is most important, so tetanus toxoid or a placebo injection should be promptly given unless systemic signs are already evident; in this event specific antivenom should be given. If a tourniquet has been applied it should be released. Unless one is confident that there is no possibility of significant poisoning ensuing, the patient should be carefully observed every half hour for some hours. If tetanus toxoid has been given initially, a second dose should be injected about six weeks later.

Initially, no covering or dressings should be applied to the site of the bite, since they greatly increase the incidence of secondary bacterial infection. Similarly, blisters should be left alone. But as soon as local necrosis is obvious sloughs should be excised. It may take several days for cobra bite necrosis to show (over a week if steroids have been given). Normal saline is the best dressing after excision of the slough. Antibiotics may now help and tetanus antiserum should be given (only for cases with necrosis—not as a routine). Skin grafting may be needed if necrosis is extensive. Pain is rarely a problem once the victim has received an injection.

Blood transfusion helps in viperine shock, especially if the victim was anaemic before the bite (but specific antivenom is usually dramatically successful in viperine shock if given in adequate dosage).

If respiratory failure develops in elapid or seasnake poisoning—shown by confusion, stupor, rapid shallow breathing, rise in pulse and blood pressure —a tracheostomy should be done. Artificial respiration and intragastric drip feeds may also be needed.

Specific Antivenom

Specific antivenom should be given only when signs of systemic poisoning are clinically evident; it should not be given as a routine in all cases of suspected snakebite. Haemorrhagic signs indicate a viperine antivenom. Neurotoxic signs without local swelling indicate mamba antivenom in Africa and krait antivenom in Asia. Neurotoxic signs plus local swelling (not due to a ligature) indicate cobra antivenom. Clinical distinction of poisoning by the various Australian and Papuan elapid snakes is difficult. Nonclotting (defibrinated) blood is a feature of taipan poisoning, whereas coagulation is normal in death adder poisoning. In some countries only polyvalent antivenom is available, so these distinctions are academic. Serum sensitivity may be tested by injecting 0.2 ml. antivenom subcutaneously; if severe reactions occur desensitization is needed before antivenom treatment.

Antivenom should always be given by intravenous drip except in mild systemic viperine poisoning. At least 100 ml. antivenom (usually contained in 10 ampoules) is needed, and this should be repeated, specially in neurotoxic poisoning, within one hour if there has been little significant improvement. The antivenom can be suitably diluted in two to three volumes of isotonic saline.

Adrenaline should be readily available for immediate antivenom reactions, which may occur despite negative sensitivity tests. Steroids are useful for delayed serum reactions, but controlled trials in human patients show that poisoning is not helped.

If antivenom is correctly used the response in systemic poisoning is dramatic. Local effects of envenoming do not appear to benefit. If it were possible to inject antivenom locally at the site of the bite *within a few minutes of the bite* necrosis might well be prevented or minimized. But in practice this is virtually never possible, and therefore local injection of antivenom is not advocated.

To be effective antivenom must, generally speaking, be specific. But recent work suggests that tiger snake antivenom (made in Australia) may constitute a "broad spectrum" antivenom effective against all commoner types of neurotoxic poisoning by Afro-Asian landsnakes and against seasnake bite poisoning. The following is a list of some institutes making antivenom suitable for snakebite in the tropics:

(1) Algeria: Institut Pasteur d'Algérie, Rue Docteur Laveran, Algiers.

(2) Australia: Commonwealth Serum Laboratories, Parkville, Melbourne.

(3) Brazil: Instituto Butantan, Caixa Postal 65, Sao Paulo.

(4) France: Institut Pasteur, Service de Sérothérapie, 36 Rue du Docteur Roux, Paris XV.

(5) Germany: Behringwerke AG, Postachliessfach 167, 355 Marburg.

(6) India: (*a*) Central Research Institute, Kasauli, R.I., Punjab. (*b*) Haffkine Institute, Parel, Bombay 12.

(7) Indonesia: Perusahaan Negara Bio Farma, 9 Djalan Pasteur, Bandung.

(8) Iran: Institut d'Etat des Sérums et Vaccins Razi, Boite Postale 656, Teheran.

(9) Japan: Institute for Infectious Diseases, University of Tokyo, Shiba Shirokane-daimachi, Minato-Ku, Tokyo.

(10) South Africa: South African Institute for Medical Research, P.O. Box 1038, Johannesburg.

(11) Taiwan: Taiwan Serum Vaccine Laboratory, 130 Fuh-lin Road, Shiling, Taipei.

(12) Thailand: Queen Saovabha Memorial Institute, Bangkok.

(13) United States: Wyeth Inc., Box 8299, Philadelphia, 1 Pa.

Doctors who need supplies of antivenom for use in various geographical areas may find the following most useful:

Americas: Polyvalent viper antivenom from 13; coral-snake antivenom from 3.

North Africa: Viper antivenom from 1, 4, or 5.

Mid Africa: Mamba antivenom from 10 (or 4); African cobra antivenom from 4, 5, or 10; viper antivenom from 4 (Bitis-Echis), 5 (Echis) or 10 (Echis).

South Africa: Mamba, cobra, and viper antivenom from 10.

Middle East: Viper-cobra antivenom from 4, 5, or 8.

Asia—Seasnake bite: Seasnake antivenom from 2.

Burma, India, and Pakistan: Cobra-krait-viper antivenom from 6 (*a*) or 6 (*b*).

Cambodia, Laos, Malaysia, Vietnam, Thailand: Viper and cobra antivenoms from 12.

Indonesia: Cobra-krait-viper antivenom from 7.

Japan: Viper antivenoms from 9.

Philippines and Taiwan: Cobra, krait, and viper antivenoms from 11.

(The figures may be seen in the original article.)

FOREIGN MATERIAL AND POSTOPERATIVE ADHESIONS *

Lauri Saxén, MD, Phil. Lic., and Hannu Myllärniemi, MD,
New Eng J Med 279 (4):200–202, July 25, 1968.

A problem of major importance in abdominal surgery is the prevention of intra-abdominal adhesions with their sequelae. It has been estimated that approximately 10 percent of repeat laparotomies are performed because adhesions have caused intestinal obstruction and, on the other hand, that in 70 to 90 percent of adhesive obstructions a connection with previous laparotomies can be established. This high frequency of adhesions and their serious consequences makes it imperative that more attention should be paid to their prevention, which can only be realized when the causative factors are known and the mechanism of adhesion formation understood. The list of factors either proved to cause adhesions or suggested as being involved includes mechanical trauma, infections, tissue ischemia, reperitonealization, thermal and chemical injuries and foreign bodies.

It is our intention here to review briefly one often overlooked and forgotten group of causative agents —namely, foreign material contaminating the peritoneal tissues. Although the frequent involvement of such foreign material in adhesion formation needs to be stressed, it should not be forgotten that it probably acts in combination with other conditions after traumatization of the peritoneum. Moreover, the importance of host factors should be borne in mind.

It is known that many types of foreign material cause "irritation" of tissues, appearing as foreign-body inflammatory reaction and formation of granulation tissue. However, we shall restrict ourselves to those shown empirically or experimentally to be causally connected with intra-abdominal adhesions.

Talc, used earlier in "wound powders" and still in some hospitals as a glove lubricant, was long ago

* From the Third Department of Pathology and the Second Department of Surgery, University of Helsinki, Finland.

shown to cause a tissue reaction indicative of irritation. In our series of 309 repeat laparotomies that demonstrated intra-abdominal adhesions, foreign-body-type granulomas were observed in 61 percent of cases, in half of which talc crystals could be detected. Another glove lubricant, starch powder, is also known to cause foreign-body-type reactions, but was detected in only two cases in the series mentioned above. It might have been the causative agent, however, in some of the 121 cases in which no foreign material could be detected at the time of reoperation, for experimental studies have indicated that this lubricant is soon resorbed but may cause permanent lesions. In addition, we have seen several cases in which starch powder has led to an acute condition with symptoms of peritonitis and a histologic finding suggesting an acute foreign-body reaction.

Gauze lint seemed to be a frequent contaminant of the peritoneum in our series and was suggested as the causative agent in 26 percent of the patients with granulomas. Some earlier observations have likewise shown a correlation between contamination with this material and the subsequent occurrence of tissue lesions and, hence, should be considered as a possible factor in true abdominal adhesions. Finally, material extruded from the digestive tract should be mentioned. Our series showed large, partially doubly-refractive bodies, apparently of vegetable origin, in some cases either as the sole finding or combined with unclassifiable foreign material.

The etiologic diagnosis of intra-abdominal adhesions should be based on histologic examination. Gross differentiation between foreign-body peritonitis on the one hand and tuberculous peritonitis or peritoneal carcinosis on the other is often very difficult, and such findings should always be followed by a biopsy. The foreign material may be detectable on routine examination as sharply demarcated, non-stainable spots or, if the material is starch granules, in PAS-stained specimens as pinkish particles with a dark dot at the center. We suggest, however, that all granulomatous lesions seen in surgical specimens should be screened in polarized light, in which foreign material is easily detectable. We especially emphasize the fact that the light intensity convenient for the eye in routine examination is not always sufficient to enable detection of minute foreign particles, and the examination should therefore be performed with light of high intensity.

In addition, it may be difficult for the pathologist to distinguish between a true foreign-body reaction and contamination during the recent operation. Intracellular particles naturally indicate a true reaction, whereas foreign material buried in masses of fibrin and leukocytes may cause confusion. In differential diagnosis, other granulomatous lesions (such as tuberculosis and sarcoidosis) have to be excluded, and in some cases, dense cellular infiltration and polymorphism of the histiocytes, together with abundant eosinophils, may suggest a neoplastic lesion. Detection of foreign particles in such lesions, on the other hand, does not exclude the possibility that other conditions are present, for we have seen typical foreign-body granulomas in peritoneal metastatic lesions.

The foreign material contaminating peritoneal tissues thus may act together with other traumatizing conditions. Our experimental results on rabbits suggest that the foreign material may prevent the fibrinous adhesions from becoming resorbed, as is usually seen after clean operations. Moreover, we know that it preferentially accumulates on peritoneal raw surfaces, the predilection sites of the fibrinous adhesions primarily formed.

By far the most important route of contamination is the surgical intervention. Major and numerous operations are associated with more frequent occurrence of foreign material. Glove lubricants and gauze lint are the most important sources of contamination. In addition, absorbable hemostatics, antimicrobial agents, especially their constituents, and sutures may all act as foreign bodies and thus promote formation of adhesions. Infrequently, peritoneal contamination followed by granulomatosis may occur through other routes, such as digestive-tract perforations, ruptures of intra-abdominal tumors or cysts and through the female genital tract.

Conclusions

At least one important cause of postoperative adhesions can be eliminated if contamination of the peritoneum by foreign material is prevented. This goal can be reached through simple measures such as washing of gloves, omission of wound powders and absorbable hemostatics and reduction of the use of gauze in the open operative field to a minimum. A clean, uncontaminated peritoneum always creates the best conditions for uncomplicated healing.

(The figures and references may be seen in the original article.)

APPROACH TO THE PATIENT WITH "IDIOPATHIC EDEMA" OR "PERIODIC SWELLING"

George W. Thorn, MD, JAMA 206(2):333–338, Oct 7, 1968.

The presence of edema implies, by definition, an increase in extracellular fluid and its principal mineral constituents, sodium and chloride. "Periodic swelling" identifies a physicopsychologic syndrome which occurs almost exclusively in adult females. It is characterized by periodic bouts of swelling and abdominal distention in the absence of demonstrable cardiac, hepatic, or renal disease or abnormalities in serum protein levels. It is often associated with headache, increased irritability, and depression. The symptoms are frequently accentuated by hypokalemia, hypomagnesemia, and postural hypotension secondary to excessive use of diuretics.

Pathophysiology

Hormones which regulate salt and water balance do so predominantly through their action on the kidney. The secretory regulation of these particular humoral agents is known to be closely related to stimuli which enter the central nervous system.

Antidiuretic Hormone.—The antidiuretic hormone, ADH or vasopressin, is an octapeptide which is secreted by neurons which arise in the supraoptic and paraventricular nuclei and terminate in the posterior pituitary or neurohypophysis. Secretion of vasopressin is monitored by changes in the solute concentration or osmolality of plasma (osmo regulation), the intravascular or extracellular fluid volume (volume regulation), and by central nervous system activity, (neural regulation).

Secretion of vasopressin has been induced in man and experimental animals by electrical stimulation of the hypothalamus and its components. Numerous centrally acting stimuli, such as noise, pain, or fright, may increase the secretory activity of the neurohypophysis whereas the administration of drugs, such as nicotine, acetylcholine, and alcohol, inhibits the secretion of ADH. Study of neurohypophyseal function has been seriously limited by the fact that the concentration of this hormone in human plasma is infinitesimally small. The estimated plasma concentration of vasopressin is no more than 5 to 10 microunits per milliliter.

The current hypothesis as to the mechanism of action of vasopressin on water reabsorption by the kidney implies that this hormone renders the cells of the distal portions of the nephron permeable to water, thus permitting the passive diffusion of tubular water along an osmotic gradient across the cell and into the peritubular vessels.

Periodic edema induced by excessive ADH secretion alone should mimic the clinical changes so well characterized by the syndrome of "inappropriate ADH secretion," vis, hypo-osmolality of the plasma and hypertonicity of the urine. Serum sodium and chloride values should be low due to excessive retention of water. These changes are not characteristic of the majority of patients with periodic edema and, hence, if excessive ADH secretion occurs in this syndrome, it must be associated with increased aldosterone secretion, which gives rise to increased sodium and chloride retention.

Aldosterone.—A second important, electrolyte-regulating hormone, aldosterone, is secreted by the adrenal cortex, but in contrast to adrenal glucocorticoids and androgens, its secretion is regulated primarily by neurohumoral mechanisms other than corticotropin (ACTH). Aldosterone provides for the homeostatic regulation of total body stores of sodium, chloride, and potassium. It acts predominantly on the distal renal tubule, including increased sodium absorption in exchange for secreted potassium as is evidenced by lowered potassium levels and increased urinary potassium excretion. Aldosterone is important in the maintenance of extracellular fluid sodium concentration and content. In its absence, extracellular fluid volume decreases rapidly.

The controlling mechanism for aldosterone release is not known. Evidence suggests that under conditions of extracellular volume depletion, sensed by pressure-volume receptors located within the arterial system, a specific aldosterone-stimulating hormone is released which, in turn, increases the adrenal secretion of aldosterone. This results in sodium retention and consequent replenishment of the volume deficit. It has been proposed that the renin-angiotension system may function as such a mediator.

From the Department of Medicine, Harvard Medical School and the Peter Bent Brigham Hospital, Boston.

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Reprint requests to 721 Huntington Ave, Boston 02115 (Dr. Thorn).

Again, as in the case of vasopressin, increased aldosterone secretion may be triggered by a wide variety of stressful stimuli.

It is possible to measure the plasma level and secretory rate of aldosterone as well as its urinary excretion. The latter ranges between 5 μg and 25 μg/24 hr, whereas plasma levels range between 5 and 15 mμg/100 ml, and secretory rates range between 50 μg and 300 μg/24 hr on ad lib diets.

If episodes of periodic edema were due solely to excessive secretion of aldosterone in response to stress or posture, one would anticipate that the administration of aldosterone-blocking agents, such as spironolactone, would be highly effective. Such is not the case in most instances although aldosterone blockade does enhance the action of other diuretics and does minimize or prevent the hypokalemia which complicates so frequently the excess use of diuretic agents in patients with this physicopsychologic syndrome.

"Third Factor".—Recently, it has been postulated that the "escape" (which occurs when salt-retaining hormones, such as aldosterone and 11-desoxycorticosterone, are administered over a prolonged period to normal subjects) is mediated by a "third factor." This factor is believed to be operative at the level of the proximal tubule, and its primary action is to decrease sodium reabsorption at this location. As a consequence, the distal tubule is presented with an excessive amount of sodium which results in (1) increased sodium escape into the urine and (2) increased potassium excretion as sodium ions are exchanged for potassium ions.

Experiments suggest that "third factor" is a humoral substance. Neither its site of origin nor its chemical structure is known. It is apparent, however, that reduced secretion of this substance favors salt and water retention. Whether a disturbed regulation of "third factor" secretion plays an important pathogenic role in cyclical edema remains to be determined.

In addition to a "third factor," it has also been tentatively suggested that there may exist a "fourth factor," a substance which may act farther along in the nephron and which, in a manner similar to "third factor," may reduce the absorption of sodium by more distal tubular cells.

Histamine and Kinins.—In considering inherent mechanisms which might facilitate salt and water retention, the family of chemical mediators, such as *histamine* and the *kinins,* which markedly affect *vascular permeability* should be included. Such substances could mediate the sequestration of considerable quantities of fluid in the extravascular compartments. For example, patients with hereditary, periodic angioneurotic edema exhibit a decreased amount of an inhibitor, normally present in plasma, of a globulin permeability factor (Kallikrein). They also lack the normal plasma inhibitor of C'1 esterase. Two patients with this syndrome have been reported who also exhibited excessive urinary excretion of histamine between attacks. Thus, three biologically active systems appear to be affected in some patients with this syndrome, viz, the Kallikrein-kinin system, the complement system, and the metabolism of histamine.

Reduced liberation of "third factor" could be an important mediator in periodic edema, particularly in conjunction with factors which increase capillary permeability and, hence, stimulate increased ADH and aldosterone secretion in an effort to restore "effective" blood volume. Under these circumstances, reduced "third factor" secretion could prevent or minimize renal loss of sodium and prevent the "escape" which otherwise might occur with sustained aldosterone secretion. To date, it would appear that periodic edema is more likely to be due primarily to changes in capillary permeability than to excessive ADH or aldosterone secretion. The latter undoubtedly play an important secondary role.

Postural Hypotension.—Two additional pathogenetic mechanisms deserve consideration. Patients with marked postural hypotension—who exhibit a marked inability to excrete a water load when maintained in the upright position during the test—obviously will have a greatly increased predisposition for edema. They will also be more refractory to diuretic therapy except insofar as mechanical contrivances can modify the extent of the postural response.

Water Excretion Test

A. With patient in horizontal position.
   1. Carried out in the morning under fasting conditions. No smoking. Patient in bed.
   2. At 8 a.m., 8:15, and 8:30, 500 ml of water (total 1,500).
   3. Patient voids at 8:30 and discards this specimen.
   4. Urine volume measured hourly for four hours.

B. With patient up and about for entire period. Test carried out as above.

Prediabetes.—Recently, Shaw and his co-workers

have suggested that an appreciable number of obese females with idiopathic edema may, indeed, exhibit an abnormality in carbohydrate metabolism and glycoprotein formation similar to that seen in prediabetes. Patients in this study were found to have elevated levels of serum insulin, diabetic glucose tolerance curves, and increased blood *fucose* levels one hour after glucose loading. Microscopic examination of biopsy specimens showed excessive glycoprotein deposits in the walls of small vessels. The authors believe that these changes predispose to capillary leakage and decreased effective blood volume which, in turn, initiate a series of responses resulting in further salt and water retention. Phenformin hydrochloride given to patients resulted in a return to normal insulin levels in six weeks, at which time treatment with diuretic agents was instituted. The authors claim that a decreased tendency to periodic edema was accompanied by a return to normal of glucose tolerance and levels of blood fucose and blood insulin. Since capillary changes might be anticipated to occur by a similar mechanism in males in whom the syndrome of "periodic edema" is rarely, if ever observed, they must be characterized as "predisposing" rather than causative. The importance of recognizing this type of pathophysiological change lies in the apparent potentially beneficial therapeutic approach which it offers to selected patients.

Abdominal Distention Without Weight Gain.—Abdominal distention or "tightness" about the abdomen is a frequent complaint of patients with "periodic swelling." This symptom may occur without excessive weight gain or edema and without evidence of intraluminal swelling of the bowel. Alvarez has suggested that this syndrome may result from relaxed abdominal musculature which, in many ways, simulates the condition of pseudocyesis.

Increased Nervous Irritability.—Excessive fluid retention is frequently associated with increased nervous irritability and, indeed, in susceptible individuals can predispose to convulsive seizures. This increased nervous irritability heightens the responsiveness of patients to disturbing emotional and psychological factors, thus tending to perpetuate or aggravate the underlying pathophysiological responses.

Diuretic therapy, if maintained for prolonged periods, may lead to *potassium and magnesium deficiency*. Since both of these ions are vital to the maintenance of normal cell membrane potential, their deficiency can increase appreciably both neural and neuromuscular irritability. It is not unusual to observe that, in the presence of potassium and magnesium deficiency, weakness and irritability can persist even though edema has been corrected!

Postural Hypotension and Diuretics.—Postural hypotension may, of course, be present initially in a number of patients with "periodic swelling." However, the excessive use of diuretics may cause unnecessary depletion of plasma volume and, hence, predispose patients to postural hypotension with its disturbing symptoms as well as its potent stimulating effect on salt- and water-retaining mechanisms.

Allergic Reactions.—Since idiosyncrasies to foods or medications can evoke an attack of generalized edema or may aggravate preexisting edema, a careful search for such possible relationships is mandatory.

Summary of Pathophysiology.—Thus, it appears that there are within the body a variety of humoral substances and mechanisms under control of the nervous system which are capable of inducing significant shifts in fluid balance. It is important that patients, as well as physicians, are aware of the magnitude and potency of this "human pharmacopeia" and appreciate the extent to which these mechanisms can be mobilized by emotional and psychological forces. In the last analysis, excessive fluid retention is mediated via renal retention of salt and water as a response to the liberation of excessive humoral agents or as a consequence of increased responsiveness to normal concentrations of these mediating factors.

Why Is the Syndrome of "Cyclical Edema" Almost Exclusively Restricted to Women?—As far as it is known, men possess the same humoral agents and pathophysiological mechanisms as women, yet cyclical edema in the absence of serious organic disease is rarely, if ever, observed. It is apparent, however, that the adult female throughout her reproductive life is subjected to a series of cyclical events, all of which place an acute demand on the organism for mineral and water retention. There is the need for blood volume replacement immediately following menstruation. Pregnancy results in the retention of large quantities of minerals and fluid, and lactation imposes an even greater demand on fluid and electrolyte turnover. Thus, the pathways and mechanisms which mediate fluid and electrolyte retention must, of necessity, be well established in the female, and the events requiring these intense metabolic changes are peculiarly related to womanhood and femaleness. It might be anticipated, therefore, that in

directing emotional and psychological stresses into physiological channels, adult females might use this primitive and essential response of salt and water retention. Not only would this be a natural pathway, but it would also provide an effective mechanism by which emotional and psychological stimuli could be translated into visible physical abnormalities.

Why particular women exhibit these phenomena is also not certain. Is their response to emotional and psychological stresses different or more intense? Are their physiological mechanisms for salt and water retention more sensitively attuned? These are questions which will require further studies. One fact is certain, postural hypotension and organic disease of blood vessels, kidney, heart, liver, and plasma proteins can magnify significantly the quantitative aspects of this response.

Diagnostic Procedures

Changes in Body Weight.—It is useful in characterizing the syndrome to obtain accurate weight measurements in the morning prior to breakfast and in the evening upon retiring. Most individuals may be expected to gain 0.5 to 1.4 kg (1 to 3 lb) during the day, with a subsequent return to the previous morning's weight after a night's rest. Patients who retain fluid excessively will, in general, gain more than 1.4 kg (3 lb) daily and if this continues, clinical edema will eventually develop. The detection of excessive diurnal weight gain is both a key to diagnosis as well as a very important means of monitoring therapy.

Blood Chemical Measurements.—Serum potassium and magnesium values are extremely important measurements for patients who have received prolonged diuretic therapy. Since many patients are often unaware of the nature or magnitude of their diuretic therapy, it is well to check serum uric acid and blood glucose as well as blood urea nitrogen levels. Hypokalemia in the presence of elevated serum uric acid level suggests excessive diuretic therapy despite a negative history! This is particularly likely to be true if mild hyperglycemia is also present. Serum electrophoresis is essential to exclude hypoalbuminemia or hyperglobulinemia. The latter might suggest underlying vasculitis as a possible diagnosis.

Tests for Renal, Hepatic, and Cardiac Function.—Renal Function.—These tests include urinalysis, including sediment and specific gravity, phenosulfonphthalein test, and renal biopsy in doubtful cases.

Hepatic Function.—Studies for hepatic function include enzyme analyses and serum bilirubin value, sodium sulfobromophthalein test, x-ray film for esophageal varices, and liver biopsy in doubtful cases.

Cardiac Function.—Electrocardiogram (ECG), chest x-ray film are taken, and venous pressure and circulation time are recorded.

Plasma Protein Studies.—Serum albumin and globulin levels should be determined with electrophoretic studies.

Water Excretion Test.—Horizontal Position.—This is carried out in the morning under fasting conditions. Smoking must be excluded. *Test:* 500 ml of water is ingested at 8 a.m., 8:15, and 8:30 (total 1,500 ml). The patient voids at 8:30 and discards this specimen. Urine volume is then measured hourly for the subsequent four hours. The maximum volume attained in any single hour is measured as well as the total percentage of ingested water which is excreted. Most normal subjects will attain a volume of at least 300 ml or more in one hour and a total of at least 80 percent to 90 percent in the four-hour period. The majority of patients with cyclical edema without underlying organic disease will exhibit a normal water excretion level in the horizontal position.

Water Test in Upright Position.—If water excretion is normal in the horizontal position, then the test should be repeated the following morning with the patient up and about during the entire four-hour period. The difference in the rate of water excretion in this position as compared to that in the horizontal position will give an overall indication in a particular patient of the importance of posture in facilitating salt and water retention. These observations will also illustrate one of the reasons why the patient may do better on a given regimen in the hospital (in bed) as compared to a similar program at home where the patient will be up and about most of the day.

Psychiatric Interview.—Evaluation of the patient's psychological and emotional status is essential in establishing the diagnosis of cyclical edema. Furthermore, such an interview is most helpful in organizing the patient's overall therapeutic program.

Summary of Diagnosis.—In establishing a diagnosis of idiopathic edema or cyclical swelling, three considerations are critical: (1) the demonstration of excessive weight gain or fluid retention, (2) the exclusion of organic disease known to predispose to edema formation, and (3) evidence of substantial psychological or emotional disturbance.

Therapy

General Considerations.—Therapy must be directed at relieving the underlying emotional difficulties as well as correcting the excessive fluid retention. The loss of edema alone can scarcely be expected to relieve symptoms significantly when the excess fluid retention resulted from a fundamental psychological disturbance. Loss of edema fluid may improve physical comfort to some extent and may reduce overall irritability, but the physician cannot hope for significant or permanent improvement from this approach alone. Moreover, since the physical stigmata of the disorder may have generated increased sympathy and attention or may have provided a means by which the patient was able to avoid social contacts or responsibilities, their removal, without improvement in the basic cause, may result in heightened anxiety.

An effective approach to the patient exhibiting this syndrome requires the identification of the major sources of anxiety, a careful explanation as to the means by which emotional stimuli can result in the release of chemical mediators which, in turn, result in excessive salt and water retention and finally reassurance that the actual weight gain can be corrected and prevented by appropriate medical therapy. With time, the syndrome tends to run out its course in most instances, and this fact can provide additional optimism. It is important for a patient to understand that *excessive* diuretic therapy may initiate an entirely new category of symptoms, such as fatigue, muscular weakness, and postural hypotension.

For most patients, a period of hospitalization initially is essential. This will provide an opportunity for carrying out diagnostic tests designed to exclude organic disease, for psychiatric consultation, for a demonstration of the importance and significance of monitoring morning and evening changes in weight, and for a more favorable situation in which to initiate a therapeutic salt-losing program. Bed rest and a low-caloric diet measurably improve the effectiveness of reduced sodium intake and diuretic therapy.

Dietary Control.—Caloric Intake.—Since obesity increases the tendency to retain fluid, the caloric intake should be restricted until ideal weight has been attained.

Sodium Chloride Intake.—A diet not to exceed 3 to 5 gm of sodium chloride is recommended for most patients since this, for practical purposes, approximates the lower level to which patients can adjust their diet at home. In very severe and resistant cases, the sodium chloride level may have to be reduced initially to 1.0 gm or less.

Fluid Intake.—There is no need to restrict water or liquid intake unless hypo-osmolality of the serum or hyponatremia exists.

Potassium Intake.—The ingestion of foods high in potassium should be encouraged especially those which are also low in sodium, such as bananas. Supplementary potassium may be administered to patients with significant depletion but, when spironolactone is used regularly and continuously, a potassium supplement is usually not required.

Antihistaminic Agents.—These may prove of value in patients with evidence of increased histamine release or allergic reactions.

Diuretic Therapy.—Spironolactone, although only a mild diuretic, is a basic medication since it (1) offsets the secondary hyperaldosteronism which almost every patient with this syndrome exhibits, (2) facilitates the retention of potassium, and (3) enhances the effectiveness of other diuretics. Spironolactone should be given in relatively larger doses during the early morning hours and during the day when the patient is up and about as this period encompasses the maximum rate of endogenous aldosterone secretion. The dosage of spironolactone should be adjusted from 25 to 100 mg four times daily.

In most patients, an additional diuretic, such as a thiazide, triamterene, furosemide, or ethacrynic acid will be required. Here the strategy is to restrict the use of the supplementary diuretic to once every three to five days in the beginning and then gradually increase the interval. The greater the interval, the greater will be the response and patients should be encouraged to make every effort toward extending this interval! For more severe cases, it may be desirable to restrict sodium chloride rigidly on the day after the additional diuretic has been given. Since "rebound retention" of sodium is unusually high on the day following the supplementary diuretic, a drastic reduction in sodium intake on this one day can often extend the need for the added diuretic by several days. A simple diet for the "very low salt day" is to limit all food to fruit and rice (unsalted); the patient may have an unlimited quantity of tea or coffee.

Correction of Postural Hypotension.—Patients who display significant retention of water when the test is carried out in the upright position will benefit from elastic stockings and may need to lie down for one to two hours in midday.

Prediabetic Patients.—Phenformin hydrochloride (25 to 50 mg daily) is given to reduce the insulin level in these patients. Experience has shown that serum insulin levels can be returned to normal usually within six weeks. At this point, diuretic therapy, as outlined above, should be instituted.

Monitoring Weight.—A careful record of the changes in daily weight, recorded both in the morning and the evening, constitutes a very important aspect of the therapeutic program. Therapy can be accurately monitored by this relatively simple device and, if plotted on graph paper, will provide an excellent basis for discussion between patient and physician. With a record such as this, the physician can be confident in predicting the changes in the therapeutic program which will be required, and the patient will be reassured by the information which the chart conveys.

Empathy.—With the help of a psychiatric consultant, the physician will be in a strong position to understand the needs of his patient, and the most effective way in which these can be met. The physician, with a comprehensive knowledge of the physiological abnormalities, must be willing to see his patient regularly and allow time for discussion.

Summary

"Idiopathic edema" or a "periodic swelling" constitutes a physiopsychologic syndrome which uniquely affects adult females. Physiological mechanisms capable of modifying salt and water metabolism within the body include the antidiuretic hormone (ADH), aldosterone, "third factor," histamine, and kinins. The intimate relationship between the secretory control of these humoral agents and the central nervous system is well established. Emotional and psychological factors are readily capable of initiating the release of these agents and, hence, of inducing cyclical retention of fluid and electrolytes. Why the syndrome is limited to the female is still conjectural; however, cyclical retention of fluid and electrolytes occurs physiologically following menstruation and during pregnancy and lactation. Thus, a well-developed pathway is available in the female for psychological disturbances to manifest themselves pathophysiologically. An understanding of the psychological and emotional factors is basic to successful therapy. Judicious use of diuretic agents can correct the physiological abnormalities in most instances, however, the basic symptoms will not be relieved by diuresis alone. Of particular importance is the avoidance of excessive diuretic therapy with its predilection for inducing potassium and magnesium deficiency which, in turn, may perpetuate the symptoms of weakness, fatigue, and irritability. The complex nature of this syndrome necessitates astute, thoughtful, and continued medical care. This therapeutic program has proved successful.

Generic and Trade Names of Drugs

Spironolactone—*Aldactone.*
Triamterene—*Dyrenium.*
Furosemide—*Lasix.*
Ethacrynic acid—*Edecrine, Endercin.*

(The figures and references may be seen in the original article.)

MITE INFESTATIONS OF MAN CONTRACTED FROM DOGS AND CATS

L. R. Thomsett, MRCVS, Brit Med J 3(5610):93–95, July 13, 1968.*

Summary.—Acarine infestations of the dog and cat are transmissible to man. The relation between age incidence in the host, duration of disease, and circumstances under which the animal is kept are stated. Fifty out of 65 human contacts at risk to 42 infected dogs and cats showed lesions of mite infestation; 48 percent of these lesions were confined to the arms and torso.

It is important to consider animal mite infestation in the differential diagnosis of human pruritic and papular skin disease.

Introduction

Mite infestations of the skin of small domestic animals which are transmissible to man are common in the United Kingdom. Human contact with infested animals readily gives rise to skin lesions for which medical advice may be sought. The purpose of this communication is to indicate the parasites

* Department of Medicine, Royal Veterinary College, North Mimms, Hatfield. Herts.
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involved in animal disease which may give rise to human infestation. With the marked increase in the incidence of human scabies it is of importance to include animal mite infestations in the differential diagnosis of human pruritic skin disease.

Acariasis in Animals

Sarcoptes scabiei var. *canis* commonly infests dogs, while *Cheyletiella parasitovorax,* a free-living mite in the hair coat of the dog, cat, and rabbit, does so to a lesser extent. Both parasites are, however, readily able to cause skin disease in man.

Notoedres cati, the counterpart in the cat of *S. scabiei* in the dog, has been recorded as the cause of a papular skin condition in man (Davies, 1941). In Britain feline acariasis due to this mite is now almost unheard of. Occasionally the condition may be encountered in cats living a semi-wild existence, and such animals rarely permit handling by man. Human infestation with *N. cati* is therefore unlikely to occur.

Direct infestation of man with the larval forms of the harvest mite *Trombicula autumnalis* is well recognized. The dog and cat are seasonally infected with this acarus and may act as mechanical vectors of it to man, resulting in human pruritic skin disease.

Sarcoptic acariasis.—This disease in the dog begins as a highly irritant papular rash affecting the thin-skinned areas of the body. The lesions, as in man, are produced by ovigerous female acari burrowing into the stratum corneum in order to lay their eggs. Self-inflicted injury by scratching, gnawing, and rubbing the sites of infestation leads to chronic thickening of the skin, exudation of serum and blood, with subsequent crust formation. Secondary bacterial infection leads to the formation of pustules.

In the absence of early diagnosis and treatment, extension of the lesions to involve the whole of the animal occurs with the development of a patchy alopecia accompanying the lesions described.

In dogs with a dense hair coat early lesions may be imperceptible on superficial examination, and, apart from pruritus, the animal is symptom-free. Not until areas of hair loss and obvious lesions become apparent do owners seek advice, often many weeks after the beginning of the disease process.

Chronic scabies associated with a low-grade infestation is common after inadequate treatment, and in untreated animals which become tolerant to the infestation it may persist for many years.

Lesions of chronic infestation are commonly confined to the fringe of the pinna of the ears and the skin of the lateral aspect of the elbows and hocks—seen as chronic skin thickening, minimal crust formation, and persistent mild itch.

As in man the pruritus associated with scabies in the dog is increased with a rise in environmental temperature and is particularly noticeable in animals kept in centrally heated homes or when they are lying in front of a fire.

Sarcoptic scabies in the dog has usually been associated with young animals, in particular puppies (Smith and Claypoole, 1967), though the average age of patients in this survey was 44.7 months, 71 percent being within the 1 to 48 months' age group.

Acariasis Due to C. parasitovorax

Infestation of the hair coat of the dog or cat with *C. parasitovorax* may or may not cause skin disease in the host, though the animal remains a potential source of infection to human contacts. *C. parasitovorax* is a free-living mite which may be distinguished from other members of the *Cheyletidae* by terminal combs on the legs. The adult mite is just visible to the naked eye. The life-cycle of this species is spent entirely within the hair coat of the host. The eggs, which are attached to the hair shafts by means of a short thread-like process, hatch in four days, and after three moults the life-cycle is completed in 34 days (Humphreys, 1958).

Lesions on the animal host vary considerably, depending on the density of infestation and response of the host. In the dog the predilection site appears to be the skin of the dorsum between the base of the neck and root of the tail, though generalized infestations occur. In the cat and rabbit the distribution is more generalized throughout the hair coat.

In the dog a mild infestation with *C. parasitovorax* leads to pruritus and hyperaesthesia of the skin of the dorsum with no other evidence of disease. Heavy infestation causes skin hyperaesthesia, persistent pruritus with scratching and self-inflicted injury, a papular rash, and excessive production of dandruff (Hart and Malone, 1958). Secondary bacterial infection is not a feature.

Diagnosis

The diagnosis of animal infestations with *S. scabiei* var. *canis* and *C. parasitovorax* depends on the demonstration of the parasite. Direct microscopical examination of skin scrapings cleared in liquor potassae is often unsatisfactory in the diagnosis of

scabies, concentration and sugar flotation procedures being more reliable.

Since *C. parasitovorax* is a free-living mite the examination of coat brushings of dandruff and coat debris is often adequate for diagnosis. In heavy infestations mites may be seen with a hand magnifier, but where infestation is minimal diagnosis may require the use of concentration methods as used in the diagnosis of scabies.

Human Infestation with Dog and Cat Mite

In the course of consultant dermatological practice at the Royal Veterinary College many cases of chronic skin disease of the dog and cat are investigated, a proportion of which are referred because of suspected human involvement. The majority of cases where human skin disease has been related to an infected animal have been investigated at the request of the owner through his attending veterinarian and not at the instigation of the owner's medical adviser.

In the investigation of animal dermatological problems it is my routine practice to determine whether owners of affected animals are suffering from concurrent skin disease and whether medical advice has been sought. In the majority of cases where human involvement is confirmed no medical advice has apparently been sought, and it is remarkable that an owner with animal scabies or a cheyletiella mite rash will endure this for a considerable time, in some cases years, before seeking a professional opinion for themselves or their animal.

In the present survey 65 human contacts were directly at risk to 42 dogs or cats kept as household pets or as part of a commercial breeding enterprise. Twenty-eight dogs were infected with *S. scabiei* var. *canis;* 12 dogs and two cats were infected with *C. parasitovorax*. All diagnoses of infected animals were confirmed by demonstration of the causal parasite. Of the 65 human contacts 50 showed lesions of mite infestation, 16 being due to *C. parasitovorax* and 34 to *S. scabiei* var. *canis*.

The incidence of human infection was related to the circumstances under which the infested animal was kept and to the animal's size. Thirty dogs of small breeds, all of which were kept within the domestic household and readily handled by both adults and children, were incriminated in the transmission of infestation from animal to man. Only one of four persons breeding dogs commercially complained of personal infestation or of infection of their staff with animal mites.

Lesions in man vary from an irritant papular rash to a severe sensitivity response with blister formation (Davies, 1941; Lomholt, 1947; Fernström and Gentele, 1960) on the arms, torso, neck, and legs. The sites of predilection are the arms and torso, in particular the waistline, usually associated with nursing affected animals on the lap. It should be noted that human infestation may occur either by direct contact with an infected animal or by migration of the parasites from the animal through clothing; immediate contact between the skin of the animal and man is not therefore a prerequisite for human infestation. The site distribution for lesions in 50 persons was:

Torso	2
Legs	2
Neck, arms, torso	4
Arms, torso, legs	5
Legs, neck, arms, torso	6
Arms	7
Arms, torso	24

Confirmation of diagnosis in man by demonstration of the causal parasite presents considerable difficulty inasmuch as *S. scabiei* var. *canis,* though producing lesions, is said not to establish itself and burrow in human skin. A similar difficulty arises with *C. parasitovorax* owing to its free-living life-cycle. Since it is only with the greatest difficulty that these parasites may be found on human skin, confirmation of animal acariasis in man depends entirely on the demonstration of the organism on the animal host.

Two examples of case histories in animal owners are given below.

Case 1

A woman purchased a small pet dog 4 months of age from a reputable supplier. The animal had the freedom of the house but had its own sleeping quarters. A contact Siamese cat was also kept. When the dog was 2½ years of age the owner complained of an intermittent papular rash on her body, arms, and legs, considered on medical opinion to be emotional in origin and treated accordingly. The condition recurred, and at each recurrence the lesions were more severe. Veterinary examination of the dog showed no lesions of skin disease though there was a tendency for the animal to scratch itself more often than normal.

This situation continued for a further 18 months, during which time the owner underwent psychiatric investigation and treatment for her skin disease, and on medical advice took a holiday with her family, accompanied by the dog. On the return journey by car, having nursed the dog, her skin disease became

severe, with lesions consisting of large blisters, widely distributed about the anterior torso, arms, and thighs. Having so definitely nursed the dog she then considered the possibility of disease acquired from the animal.

Examination of the animal by her veterinarian showed little other than hyperaesthesia of the dorsal skin and small accumulations of bran-scale dandruff and a small area of dorsal alopecia. The dog was referred to me for further investigation. Examination of the animal showed it to be a well-nourished 4-year-old male pug dog. Apart from an area of hair loss approximately 2 cm. in diameter over the dorsal midline between the scapulae, bran-scale dandruff, and a rather more than normal tendency to moult, little of significance was noted. Manipulation of the hair tips over the dorsum and flanks showed significant skin hyperaesthesia with reflex scratching, a feature of canine infestations with *C. parasitovorax*. Coat brushings and skin scrapings taken from the affected area of the dorsum showed large numbers of *C. parasitovorax* in various stages of its life-cycle. Eggs of this parasite were demonstrated on epilated hairs. Repeated treatment of the dog with Tetmosol (monosulfiram) soap was prescribed, and the infestation cleared within three weeks.

The owner, of her own volition, bathed herself with the same preparation, and instructed all other members of her household to do likewise. She sent her clothing for dry-cleaning, together with such house furnishings with which the dog had been in contact and were removable. The dog's bed was destroyed. Within one week she was symptom-free and has subsequently remained so.

Case 2

A woman purchased a puppy which was subsequently given the freedom of the house. The dog showed evidence of a papular rash on the abdomen which spread to the limbs; lesions later became crusted and a patchy alopecia with persistent pruritus became an established feature of the condition. The woman's son was permitted to have the dog in bed with him, and was found by the parent to be affected with an irritant papular rash of the body, arms, and legs, particularly the upper chest. The woman was similarly affected on the forearms and around the waist.

Treatment for the dog's skin disease had been carried out on the advice of the owner's veterinarian, but owing to the suspected human involvement the animal was referred to the Royal Veterinary College for a further opinion and investigation.

Examination of the 5-month-old male puppy showed papular and crusted lesions affecting the whole of the body and limbs. There was a patchy alopecia with excess moulting of hair. Pruritus was a significant symptom, and areas of lichenified skin with accumulated dandruff were evident on the flanks and hindquarters. Skin scrapings confirmed the condition as sarcoptic scabies.

Treatment of the animal with benzene hexachloride shampoo was instituted, and the owners were advised to avoid contact with the dog as much as possible until the condition was cured. Spontaneous remission of the human skin disease was subsequently reported.

Differential Diagnosis of Acariasis in Animals and Man

Human infection with the skin parasites of small domestic animals, though recognized, is rarely considered of importance. Smith and Claypoole (1967) suggested that there is a need for closer consideration of such forms of parasitism in the differential diagnosis of papular and vesicular skin disease in man; that this is so is borne out by the experience reported here. With a population of at least 10 million dogs and cats, approximately 50 percent of each species, kept in households in the United Kingdom and an incidence of parasitism with *S. scabiei* alone in the dog of approximately 1 percent—that is, 50,000—one would anticipate the number of human cases to be significant.

The problem of the differential diagnosis of scabies in the dog is less difficult than in man. Since in the majority of cases in the dog the acarus has a predilection for the fringe of the pinna of the ears, a scratch reflex can be elicited on manipulation of this site which is pathognomonic of scabies. In the few cases where the ear is not involved, and in cheyletiella infestations of both dog and cat, differentiation between parasitism due to other organisms and other papular rashes or disorders which give rise to excess dandruff present difficulty. The confirmation of mite infestation therefore depends finally on the demonstration of the causal parasite. Skin disease in the dog and cat of emotional origin is of little consequence, though scratching and self-mutilation may be associated with boredom.

In man differential diagnosis of skin disease contracted from animal contact presents greater problems, for neither *S. scabiei* var. *canis* nor *C. para-*

sitovorax is readily demonstrable in man. Lyell (1967) discusses specific differentiation of pruritic skin disease, and states that emotional factors among others are readily invoked as the cause of pruritus in man. For the purpose of differential diagnosis it should be borne in mind that, though this communication deals only with mite infestations of the dog and cat, other domestic species—for example, cage birds, poultry, and horses—may also be vectors of arthropods able to cause papular skin disease in man.

Treatment

It is obvious that treatment of the offending animal or its banishment from the household is much to be preferred to treatment of the owner with tranquilizers, sedatives, antihistamines, or even the consultant psychiatrist's couch.

(The figures and references may be seen in the original article.)

QUALITY ASSURANCE AND PHARMACOLOGICAL EQUIVALENCY

*CAPT Solomon C. Pflag, MSC USN *, Milit Med 133(6):486–490, June 1968.*

The procurement of drugs by the military is a complex and complicated undertaking which includes operating within the rules described by the Armed Services Procurement Regulations. In an effort to procure quality drugs, which certainly is the objective for the successful treatment of the sick and wounded, the role of quality assurance becomes a most significant factor. Although quality assurance is a common expression, used widely in many industries we believe that personnel intimately acquainted with the medical profession and the drug industry have a special feeling and understanding for and of this concept. We believe that quality assurance, as applied in the drug industry, is a definitive plan, organized by the technical staff of a pharmaceutical company, to assure that the formulation, manufacture, inspection, packaging, and testing of pharmaceuticals are performed within prescribed standards.

Thus, the necessary know-how, background, and experimentation that will assure a final product consistently meeting the desired characteristics of purity, quality, strength, uniformity, and stability are ensured for each item. From appropriate records, which are inherent in quality control, it is therefore possible to determine, from the lot number of a finished product, all pertinent data of the item, including the source, quantity, and lot number of each ingredient, the names of persons formulating the item, the method of manufacture, the individuals responsible for each major operation including the labeling and packaging, and the results of retained or shelf sample testing. With this concept in mind we at the Defense Personnel Support Center developed the following quality assurance program. We refer to it as the Ten-Point Quality Assurance Program. This program is comprised of the following elements: Specifications, Pre-Award Survey, Pre-Award Samples, Production Testing, Review of Inspection Data and Test Results, Laboratory Analysis, Depot Surveillance, Complaint Evaluation, Customer Liaison, Pharmacologic Testing.

Specifications

Our quality assurance program is supported by sound specifications. These specifications are based on the characteristics and attributes which the Defense Medical Material Board furnishes to the Defense Personnel Support Center in order to satisfy medical professional needs. Using these characteristics, the Technical Operations Division of the Directorate of Medical Materiel drafts specifications which will permit the acquisition of the items possessing the quality required by the military services. The data for such specifications are obtained from various compendia; from the Food & Drug Administration utilizing our Intra-Governmental Advisory Council on Drugs affiliation; from available literature; from

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* Defense Personnel Support Center, 2800 S. 20th St., Philadelphia, Pa. 19101.

in-house knowledge derived from experience with the same or similar items; and from those producers who have been supplying the item to the Services and whose item has been found acceptable by the physician. Such data, after careful evaluation and analysis to determine relevancy and reasonableness as it pertains to assuring acquisition of quality materiel, form the basis for our specifications.

Specifications are reviewed on a continuing basis and strengthened as required. This program of continuing evaluation not only utilizes the sources upon which the specification was written, but also the test results, reports and information garnered from our contract inspection system, and from information received from the field and storage personnel. Improved specifications better define Government requirements and thus the opportunity for bidders to compete is improved. We have endeavored and shall continue to strive for specifications which require a minimum of interpretation.

We have been often asked why our specifications require special requirements. Special standards are required primarily because we are involved with the world-wide distribution of medical materiel, which may be subjected to extremes in climatic conditions, such as the heat and humidity of the tropics or the subfreezing temperatures of the Arctic regions. Second, we buy for long-term storage for mobilization purposes, for prepositioned stocks, and for use in major and minor assemblies. For example, the uncommon characteristics of items to be used in the field in support of military operations impose special packaging and packing requirements. Most medical materiel, due to its intrinsic characteristics, requires Level "A" packaging, or, as we say, "maximum protection." Surgical instruments must be protected to prevent damage to critical cutting edges, or to prevent corrosion. Sterile items must have proper package barriers to prevent the entry of bacteria or water, and to minimize mechanical puncture. In the drug area, a fundamental requirement exists that items be protected from light, moisture and breakage. Therefore, proper bottles, seals, closures and cushioning materials must be specified.

Pre-Award Surveys

Our second point and one of the major levers used by the military in the quality assurance effort is the Pre-Award Facility Survey. Prospective contractors who have not manufactured the same or similar items are inspected to determine their quality control system and housekeeping standards. Our results since 1962 indicate that a large proportion of these surveys result in ultimate rejections of offerers due to quality control of housekeeping deficiencies. They simply have failed to meet acceptable standards.

Pre-Award Samples

Similar results have been obtained in the Pre-Award Sample portion of our quality assurance program. Prospective offerers who have not manufactured the same or similar items are requested to furnish samples of their product before a contract is awarded. Despite the fact that the prudent and thoughtful manufacturer would be expected to furnish us with the best product which he would preselect and test, a large number of samples still continue to fail. Each should have contained 1,000 tablets of drug "X." Upon laboratory examination, it was found that one bottle contained drug "X," but it failed to meet our specifications. The other bottle contained an entirely different drug. Note the different shaped tablets. How could this happen? The answer, simply stated, is "A complete quality control breakdown." The manufacturer was disqualified for this contract.

Production Testing and Review of Inspection Data

Our production inspection and review of inspection data have been a bulwark to our quality assurance program. It is here that we make certain that raw materials are tested, in-process controls are carried out, and proper check-tests such as weight variation, disintegration, hardness, solubility, particle size, viscosity, clarity and net weight are performed. This is accomplished by a Defense Contract Administration Services Inspector, in conjunction with the Defense Personnel Support Center Quality Control personnel, as required. Occasionally, as a result of a field complaint or because of a verification test result, we find that an inspector has not adequately performed this inspection function. Prompt and effective action is taken by Technical Operations Division Directorate of Medical Materiel. By way of illustration, several field complaints were received on medical instruments manufactured by a certain medical instrument company. Although the complaints were all on different instruments—towel forceps, two types of hemostat forceps and two types of suture needle holders—they were all on recently delivered material and cited essentially the same deficiencies in style, design, workmanship and finish. Examination of complainant and depot samples substantiated the complaints. The types of de-

ficiencies indicated a breakdown of the company's inspection control system, and raised doubt as to the adequacy of the Defense Contract Administration Services Inspector's verification inspection.

We took action to suspend all the material, the contractor was put on notice under the warranty clause of the applicable contracts, and the Defense Contract Administration Services Region personnel were advised of the complaint. I want to emphasize that, while such cases occur, they are random and sporadic.

Laboratory Analysis

The services of Government laboratories are also available for quality assurance and verification testing. In addition to our Laboratory in New York, our laboratory capability is augmented by other Government laboratories. For example, each lot of certified antibiotics, such as tetracycline and chloramphenicol, is submitted by the manufacturer to the Antibiotics Division of the Food & Drug Administration for certification. In like manner, the National Institutes of Health (NIH) approves each lot of practically all biologicals before release.

Depot Surveillance

When medical materiel is accepted by the inspector and shipped to our depots throughout the country, a systematic surveillance system is actuated. This is commonly referred to as our In-Store-Quality Control Program. Definite guidelines have been established, covering such points as cyclic inspection periods, shelf life, and serviceability standards (signs of deterioration). If signs of deterioration are noted during depot inspection, samples are sent to us for testing. Material which fails to meet our standards is suspended from issue and use.

Complaint Evaluation

What effect have these seven procedures produced on our complaint history? A most salutary effect, indeed, if we are to use our complaint history as an index of our performance. Our Type I complaints result from material which has been determined by use or test to be harmful or defective to the extent that continued use may cause illness or death. Type I complaints, both confirmed and unconfirmed, have steadily declined in the last few years. This year we have had only four Type I complaints, none of which has been confirmed. Thus, mathematically speaking, a definite reciprocal effect has been noted, as the effective result of our quality assurance program.

Customer Liaison

Supplementary to complaint evaluation, we have what we refer to as customer liaison visits. We make quality check visits to the field activities where "eye-ball" to "eye-ball" we solicit comments on medical materiel, recognizing the reluctance on the part of most people to place complaints in written form. Our director has traveled to Southeast Asia several times and in the United States extensively. Our results indicate a high degree of customer satisfaction with medical materiel. This satisfaction certainly might be expected to make us somewhat complacent. But the contrary is nearer the truth. In our "Quest for Quality Pharmaceuticals" we found that we had to go one step further to complete our Ten-Point Quality Assurance Program. Therefore a few months ago the Department of Defense approved the concept of requiring proof of pharmacological equivalency.

Pharmacologic Testing

The literature is replete with studies on factors, both biological and physico-chemical, influencing the biological activity of drugs and drug products. A representative list compiled by the National Library of Medicine includes dissolution rates, disintegration rates, comparison of dosage forms of the same drug, and particle size, as they affect biological activity; also blood tissue levels, absorption rates and metabolism, and excretion rates for drugs. This, in addition to our complaint history on a score of select pharmaceuticals, indicated a dire need for pharmacological equivalency testing.

In essence, the Defense Personnel Support Center will formulate a proposed testing procedure with the cooperation of Government personnel, universities or industry. This procedure will be submitted to the Defense Medical Materiel Board for professional evaluation and approval. The Defense Personnel Support Center will include the pharmacological equivalency testing procedure in the specification. We will also document the bidder's or offerer's method of manufacture, specifications, procedures, and quality control for the production of the specific lot of material subjected to the testing required in the specification. We will refer subsequent results of pharmacological equivalency tests performed by the bidder to the Defense Medical Materiel Board for evaluation and acceptance.

Upon acceptance by the Defense Medical Materiel Board, the product offered to the Government on

contract will be evaluated by the Defense Personnel Support Center to determine that it was produced by the same methods of manufacture, procedures, and quality control as the materiel which was found acceptable after testing. Thus the effectiveness of the contractual materiel should be equal to the effectiveness of the test samples.

There is nothing very new about testing in our procedures. On a very limited basis we have conducted such tests in the past, in the case of nitrofurantoin, and assured ourselves that the drug will achieve the desired therapeutic benefit with a minimum of toxicity or harmful side effects. It is a well known fact that matters of drug purity and potency are ascertained by chemical and biological testing. It is not practical or even desirable to subject each batch of a drug dosage form to pharmacological equivalency testing. If lot to lot consistency or uniformity is achieved by the judicious application of quality control, and if a manufacturer has presumptive evidence that subsequent lots can be correlated back to the original batch that was pharmacologically tested, there is often no need for testing each subsequent batch in this manner.

This has been a brief insight into the military requirements for quality medical materiel at the Directorate of Medical Materiel; what we are doing and what we are planning to do with regard to pharmacological equivalency testing. We will continue to exert every effort to insure the delivery of pure, safe, and effective drugs under a competitive procurement system.

(The figures may be seen in the original article.)

MEDICAL ABSTRACTS

HYPERBARIC OXYGENATION: CURRENT CONCEPTS

W. F. Bernhard, MD, and R.M. Filler, MD, Amer J Surg 115(5):661–668, May 1968.

Medical interest in oxygen therapy under increased environmental pressure dates back over 125 years, and followed Tiger's development of the caisson in 1841 as an aid to underwater construction work. In that era, pressure chambers were available in many European cities for the treatment of patients with pulmonary tuberculosis and other chronic infections, without demonstrable results. A second wave of interest in pressure therapy developed in 1878 after the investigations of a French physiologist, Paul Bert, who published the first scientific treatise on the effects of oxygen and inert gas ventilation under hyperbaric conditions. The next year, 1879, an anesthesiologist named Fontaine observed that the administration of low concentrations of nitrous oxide and oxygen under pressure resulted in excellent abdominal relaxation along with a superior degree of oxygenation of the patient. Fontaine's plan was to construct an operating theater within a pressure chamber to permit administration of nitrous oxide to patients undergoing abdominal surgery; however, this ingenious scheme never reached fruition.

Additional progress in hyperbaric medicine was stymied by the high incidence of "bends" and air embolism which followed too rapid decompression after deep and prolonged dives. However, when the British scientist Haldane formulated the concept of staged decompression and assembled the first decompression tables (1907), diving and experimental work under pressure was finally placed on a firm foundation. In 1934, United States Naval medical officer, Albert Behnke, began a study of oxygen inhalation in volunteer divers during dry dives in a compression chamber. This classic work, carried out at the Harvard School of Public Health in Boston, Massachusetts, established the maximal tolerance of man for 100 percent oxygen breathing at pressures of 15, 30, and 45 pounds per square inch gauge (p.s.i.g.).

During the past decade, clinical investigations utilizing hyperbaric oxygenation have been undertaken by Illingworth, Smith and co-workers in Glasgow, Scotland and Brummelkamp, Boerema, and Hogendijk in Amsterdam, Holland. These surgeons and their associates treated patients with carbon monoxide poisoning, anaerobic infections, and peripheral arterial occlusive disease, using oxygen administered by face mask at pressures of 15 to 30 (p.s.i.g.). Preliminary reports of their work revived interest in this subject in both Europe and the United States.

Since that time, numerous scientists and engineers have clamored for the widespread construction of clinical hyperbaric facilities in this country. Fortunately, the expense of hyperbaric equipment and the recognized dangers of acute toxicity have resulted in reasonable restraint within the medical community. The wisdom of this course of action has become increasingly apparent since little evidence has been generated to indicate that hyperbaric oxygenation is superior to the usual methods of oxygen administration in many of the clinical situations for which benefit has been claimed.

THE EPITHELIUM IN WOUND HEALING

Walton Van Winkle, Jr., MD, Surg Gynec Obstet 127(5):1089–1115, Nov 1968.

The epithelial surfaces of the body are more subject to trauma than any other tissue. Fortunately, epithelium also has a great capacity for regeneration. Functionally the epithelium acts as a barrier between the body and its environment. However, it is not a passive barrier since it selectively absorbs needed environmental materials, including radiations, and excretes toxic and waste products as observed by Rushmer. It also performs specialized secretory functions designed to assist the body in maintaining an internal homeostasis or in preparing external materials for absorption into the body.

Only the barrier function and its restoration after trauma are considered in this review. In considering the regeneration of epithelium, certain fundamental and important concepts are reviewed because their manifestations have been studied largely in relation to epithelial regeneration. These are cell migration, the initiation of mitosis, and the question of the existence of a so-called wound hormone.

The epidermis, derived from ectoderm, is the most readily accessible epithelium in the body, and much of the investigative work deals with the restoration of epidermal integrity. The epithelial lining of the intestinal tract and of the respiratory tract, derived from entoderm, presents some special problems in healing, partly because of the nature of its environment and partly because of the consequences of any abnormal healing. The same is true for the epithelium of the urinary tract, which is derived from mesoderm. The epithelial cells in each of these areas also differ morphologically and functionally.

ORTHOPEDIC SURGERY IN MANAGEMENT OF RHEUMATOID ARTHRITIS

Philip H. Davis, MD, Med Clin N Amer 52(3):717–731, May 1968.

Rheumatoid arthritis is a systemic disease of unknown etiology which primarily involves peripheral joints in a potentially destructive process. Proper treatment involves not only accurate diagnosis but thoughtful medical management coupled with adequate physical medicine and constant orthopedic evaluation. Persistent synovial thickening is usually an indication for synovectomy. This tissue acts much like malignant tissue in its local invasiveness and destructiveness. Articular cartilage loss and periarticular damage is irreversible, and should be prevented. Damage to a joint may set the stage for subsequent mechanical incongruity, stress breakdown and deformities. Surgery may offer relief to disability produced by a severely damaged joint.

GALLSTONES

Donald M. Small, MD, New Eng J Med 279(11):588–593, Sept 12, 1968.

For nearly a century and a half stasis, obstruction and inflammation have been mentioned in the literature as etiologic mechanisms in cholelithiasis. Although these concepts are important and may contribute to a particular mechanism of stone formation, general theories based on any one of these phenomena cannot explain the overall process of gallstone formation. Of prime importance is the obvious fact that normal bile is a liquid, whereas bile from subjects with cholelithiasis of any type has been altered so that solid components (the stones) and liquid bile are simultaneously present. The purpose of this report is to reclassify and summarize mechanisms of both clinical and experimental gallstone formation and perhaps to suggest direction for further research. The references have been chosen because of the completeness of their discussion or bibliography.

ASCARIS PNEUMONIA

A. P. Gelpi, MD, and A. Mustafa, MD, Amer J Med 44(3):377–389, Mar 1968.

The clinical picture of Ascaris pneumonia is described, together with observations on the endemic

occurrence of this condition among the Arab population of Eastern Saudi Arabia. The disease is an acute disorder of the lower respiratory tract presenting with cough and malaise, and in its severe form with chest pain, dyspnea and hemoptysis. Pulmonary infiltrations and a moderate eosinophilic leukocytosis identify the condition as a type of Loeffler's syndrome. The outcome among Saudi Arabian patients invariably has been favorable with the application of symptomatic measures; however, in severe cases the use of adrenal corticosteroids and oxygen may be indicated because of the alarming degree of respiratory distress.

The most reliable diagnostic criterion has been the finding of typical third-stage larvae in the sputum or gastric aspirate of suspect patients. Serologic tests, employing whole worm antigens, have not proved helpful in diagnosis under the conditions of the reported study.

The pathogenesis of the condition is believed to be a response of hypersensitivity to highly allergenic components of Ascaris larvae. The pneumonia is analogous in its clinical features, and presumably pathogenesis, to the Loeffler's syndrome which develops during treatment of Manson's schistosomiasis with trivalent antimonials.

The epidemiology of ascariasis under climatic conditions prevailing in temperate zones or arid areas in the tropics seems to determine the expression of the larval state of infection. Interruption of the infectious cycle by adverse climatic factors is likely to be associated with seasonal outbreaks of Loeffler's syndrome.

HALO NEVI

MAJ D. M. Wayte, RAMC, and E. B. Helwig, MD, Cancer 22(1):69–90, July 1968.

The clinicopathologic features of 108 halo nevi removed from 100 patients are presented, as well as a review of the previous reports on this subject. The term "halo nevus" is used to describe a pigmented nevus surrounded by a zone or margin of depigmented skin and having a life history that includes the centripetal extension of the depigmented halo and the spontaneous disappearance of the nevus. This process is most commonly found on the trunk of young Caucasian persons; it does not appear to be directly related to vitiligo but may be related to actinic radiation. The microscopic features consist of a nevus cell nevus, usually compound in type and infiltrated and surrounded by lymphocytes and histiocytes. The halo area has dopa-negative clear cells at all levels of the epidermis; electron microscopy has shown these to be Langerhans' cells. Differentiation of halo nevus from malignant melanoma and inflammatory dermatoses is presented.

PENETRATING WOUNDS OF THE HEART

W. L. Sugg, MD, et. al., J Thorac Cardiov Surg 56(4):531–543, Oct 1968.

An analysis of 459 penetrating wounds of the heart has been presented.

Eighty-six patients arrived alive in the emergency room, whereas 373 were dead on arrival, for a prehospital mortality of 81 percent. Eighty percent of the DOA cases were due to gunshot wounds which reflects their more severe nature in comparison with that of stab wounds.

Left ventricular injury has a dismal prognosis, with less than 2 percent of the patients reaching the hospital alive; four fifths of this small group die in spite of treatment.

Prior to 1966, primary treatment was repeated pericardiocenteses. An analysis of 18 deaths occurring with this treatment show that 10 were due to recurrent tamponade.

For the past 2 years, immediate operation has been the primary treatment. The mortality rate has been lowered from 36 percent for the 7 years prior to 1966 to 14 percent for the past 2 years. The mortality rate from stab wounds, which was 36 percent in the earlier period, decreased to 5 percent.

This experience supports the policy that immediate operation should be the standard treatment for cardiac wounds, with cardiopulmonary bypass and circulatory assist devices on stand-by for use when necessary.

SIGNIFICANCE OF AN ELEVATED SERUM AMYLASE

J. T. Adams, MD, et. al., Surgery 63(6):877–884, June 1968.

Of 154 patients with abdominal pain and hyperamylasemia, nearly 75 percent demonstrated isolated or associated pancreatitis, while in the remainder there was no apparent pancreatic lesion.

In general, the serum amylase level was *inversely* related to the severity of pancreatic disease. When the amylase was over 1,000 Somogyi units, there was usually a surgically correctable lesion, most frequently acute calculous disease of the biliary tract, while pancreatitis, if present, was of minimal or moderate extent. In contrast, when the amylase activity ranged between 200 and 500 Somogyi units, the majority of patients had isolated idiopathic or "alcoholic" pancreatitis; all instances of necrotizing or hemorrhagic pancreatitis were in this amylase range.

The serum amylase is an important adjunctive measure in the management of a patient with abdominal pain. Markedly elevated levels, coupled with continued clinical manifestations, should prompt early operative intervention, while minimally elevated levels suggest that, unless clinical consideration dictates otherwise, the operation should be delayed.

HOSPITAL ADMINISTRATION SECTION

HUMAN EFFECTIVENESS IN THE NAVAL SERVICE

*LCDR Paul D. Nelson, MSC USN.**

The broad mission of the naval service requires the members therein to adjust and function effectively in nearly every type of environment known to man, ranging geographically from below the North Pole to atop the South Pole and characterized functionally by special missions of field/amphibious, aviation, and underwater forces on the one hand to the relatively large communities of men confined to the boundaries of ships at sea on the other. It is towards physical and mental fitness, behavioral adjustment, and performance efficiency within those environments that the Navy Bureau of Medicine and Surgery's research and development program in Human Effectiveness is directed.

Despite the relatively high calibre of personnel input to the naval service, costs attributable to impairment of human behavior are incurred each year. Approximately 100,000 out-patient consultations and 9,000 hospital admissions are annually attributed to neuropsychiatric disorders. An estimated 15-20% of enlistee cohorts can be expected to have their first enlistment prematurely terminated as a result of maladjustment to military service. In highly specialized and select programs, such as aviation, 10-15% annual voluntary attrition is often realized in training programs alone, not to mention the even greater costs incurred when voluntary withdrawal or behavioral impairment occurs in the fleet. Finally, as the Navy ventures into such new frontiers as deep sea diving, many of the human behavior problems are as yet virtually unknown.

Bureau of Medicine and Surgery laboratories responsive to present and anticipated problems of human effectiveness consist of the Naval Aerospace Medical Institute, Pensacola, Florida; Navy Medical Neuropsychiatric Research Unit, San Diego, California; Naval Medical Research Institute, Bethesda, Maryland; and the Submarine Medical Research Laboratory, Groton, Connecticut. Four program objectives integrate the research efforts of those laboratories:

(a) to identify the personal and environmental characteristics associated with the onset of neuropsychiatric disorders and to evaluate the effectiveness of methods by which such disorders are managed and treated;

(b) to identify combinations of physical, attitudinal, and behavioral characteristics which are valid predictors of adjustment in different naval environments, to be used in addition to technical aptitude measures for selecting men for duty in aviation, underwater, and various shipboard and field assignments;

(c) to identify personal, interpersonal, and environmental characteristics related to effective small crew performance such that future vehicle design, crew composition, crew training, and crew management decisions can be facilitated;

(d) to determine effects imposed on perceptual, psychomotor, cognitive, and emotional functioning by variations in gravitational forces, barometric

* The author presently serves as Program Manager, Human Effectiveness Program, Research Division, Bureau of Medicine and Surgery.

pressures, atmospheric gas mixtures, and abnormal temperature, light, sound exposures, sleep deprivation, and work-rest cycles.

Studies recently of note in the area of psychiatric epidemiology include the collection of demographic, medical record, and personnel management data on NP out-patient consultees and admissions to NP services of naval hospitals, with follow-up studies of adjustment among those individuals returned to duty after hospitalization. That study, now in its third year, is being supplemented by the collection of general health change data on complements of shipboard personnel during full sea-duty deployment cycles. A rather unique study now in its third year is the longitudinal evaluation of the "single-seizure" case in which sudden loss of consciousness is accompanied by no apparent medical explanation. Finally, a study recently completed on the effectiveness of mass psychiatric screening procedures used in Navy and Marine Corps recruit depots yielded information supportive of the first major change in such procedures since World War II.

Selection research has been highlighted in recent years by development of an actuarial prediction system for monitoring and forecasting the effectiveness of naval aviation trainees, a development estimated to save the Navy $2,000,000 per year in aviation training costs. That effort is currently being expanded to differentiate among trainees in various branches of aviation and towards further validation in fleet operations, including combat. Using the same model, sequential predictors of military adjustment potential are being developed for Navy and Marine Corps enlistees based upon longitudinal studies of approximately 25,000 recruits from those services. Combat adjustment has similarly been studied among samples of those enlistees. Development of selection methods for such special assignments as submarine, diving, and Antarctic station duty parallel those larger studies.

As a derivative of several years of research on small groups operating under environmental restriction such as found in isolated Antarctic outposts and special underseas vehicles, a laboratory program has been developed to investigate in an experimentally controlled manner the impact of sensory deprivation, spatial confinement, and group composition and structure on emotional stability, problem-solving, and interpersonal coordination. That work has recently been extended in application to studies of the Navy's SeaLab operations.

In the area of psychophysiological functions, new directions are being taken to ascertain individual differences in vestibular functioning as related to problems of human disorientation in aerospace and underwater environments, as well as new studies of visual, auditory, and psychomotor functions in deep dive swimmer operations. In order to better understand the stresses induced in aircraft environments by physical threat and both decision-making and motor coordination requirements, new studies of aviator performance are underway using experimental test facilities on-line with computer for real-time feedback. And, with a recently established psychophysiology laboratory for the study of central and autonomic nervous system functions, effects of varying quantities and qualities of sleep deprivation on human performance and health will be extensively evaluated.

In summary, the Navy Bureau of Medicine and Surgery's human effectiveness research program is oriented towards preventing both the gross impairment of human behavioral functions and the chronically deleterious effects from man/environment transactions which render men episodically unreliable in performance of their jobs.

DENTAL SECTION

SUBJECT ACCEPTANCE OF STANNOUS FLUORIDE TREATMENT

CDR W. R. Shiller, DC USN, and CAPT F. P. Scola, DC USN, Dent Abs 13(11):670, Nov 1968.

Of 370 subjects receiving various forms of stannous fluoride treatment in a preventive dentistry program at the Submarine Medical Research Laboratory, New London, Connecticut, and subsequently interrogated by questionnaire, 307 (83%) said they appreciated getting the treatment, 8 (2%) said they didn't really want to have it, 54 (15%) said they didn't care one way or the other, and 1 subject did not respond to the question.

Fifty-nine percent of the subjects said the stannous fluoride material did not taste bad, 32% said it tasted bad, and 5% said it tasted very bad.

Eight percent said the stannous fluoride taste dis-

appeared immediately after the treatment, 43% said it lasted less than one hour, 43% said it lasted more than one hour but less than one day, and 3% said it lasted a long time.

Fifty-four percent said the treatment had no effect on their gingiva, 15% said it made their gingiva feel good, 19% said it made their gingiva hurt during the treatment, and 9% said it made their gingiva hurt for several days.

Two percent said the treatment did no good, 4% said it gave them strong teeth, 35% said it helped prevent tooth decay, 7% said it gave them strong gingiva, and 50% said they didn't know.

Thirty-three percent of the subjects said that if they were in civilian life they would have the stannous fluoride treatment if they had to pay for it, 18% said they would not, and 47% said they didn't know.

The responses indicated some aversion on the basis of taste and gingival effects to the materials used. The effects reported were not considered to be severe enough or frequent enough to recommend any significant change in the present stannous fluoride program. Acceptance of the treatment was found to be closely related to the patient's belief in its effectiveness. More effort should be expended in educating the recipient population concerning the benefits of the stannous fluoride program.

The subjects were assigned to five treatment groups. Group A received the three-agent stannous fluoride treatment applied by an operator. This consisted of a prophylaxis utilizing 8.9% stannous fluoride in prophylaxis paste, a 15-second topical application of a 10% aqueous solution of stannous fluoride, and home use of a stannous fluoride dentifrice. Group B was treated in an identical manner except that all materials were placebo, containing sodium chloride in place of stannous fluoride. Group C received the same treatment as Group A except that the prophylaxis was self-applied. Group D received treatment identical to Group C except that all materials were placebo, and Group E received the same treatment as Group C minus the interproximal taping with dental floss.

(Shiller, William R., and Scola, Francis P., Naval Submarine Medical Center, New London, Groton, Conn 06340. Subject acceptance of stannous fluoride treatment. J Oral Ther 4:388–394, Mar 1968.)

PAPASE^{R} AS A ROUTINE PREMEDICANT IN SURGICAL EXODONTIA

LT Roger E. Alexander, DC USN.

Among the new proteolytic enzymes is an extract of the plant "Carica papaya," marketed as Papase^{R}. Dentally, there have been few clinical or laboratory studies of Papase^{R}. Published studies have been subjective in nature, rather than objective. This study attempted an objective evaluation of Papase^{R} as a routine premedicant in surgical exodontia of impacted third molar teeth. The attempt was not entirely successful.

The general attitude derived from an extensive review of the literature is that the "evidence supporting the use of enzymes in man is deficient and the burden of responsibility for providing these effects remain on those who advocate their use."

In this study, fourteen patients underwent surgical removal of bilaterally-identical impacted mandibular third molars. One side served as a control side; the opposite side was performed with Papase^{R} as a premedicant. In four patients, it was felt Papase^{R} improved the healing sequence, and in four patients, it was felt the enzyme hindered the healing. In the remaining six patients, it was felt there was not significant clinical difference between the two sides. Since it was felt that subjective statements need to be replaced by objective measurements, this study, as originally planned, intended to use only measurements. Trismus was measured with a Vernier calipers as the maximum opening distance between maxillary and mandibular incisors. A specially designed and constructed facial measuring device was to measure increases and decreases in facial edema.

Evaluation of enzymes is difficult, due to the lack of precise techniques for objectively measuring the degree of edema and inflammation. Indeed, in this study it was found that facial edema was too widespread to be accurately measured. Therefore, midway in the study it was necessary to abandon the facial measurements and revert to subjective statements. It is intended to repeat this study in the future, using barium outlines and cephalometric radiographs to objectively evaluate the resolution of edema.

Several pertinent questions were raised as a result of the findings in this study, plus information in the literature.

(1) Do enzymes interfere with the normal healing mechanism?

(2) Are we actually hastening the resolution

of edema, or merely spreading it over a larger area? This study had several instances of extraoral ecchymosis on the enzyme side, indicating the contents of the tissue spaces may have spread.

(3) Will Papase[R] patients exhibit hemorrhage problems postoperatively? Other studies indicate that proteolytic enzymes can cause coagulation defects due to defective fibrin polymerization.

(4) Once a clot is formed, will Papase[R] contribute to its breakdown, since the clot is basically a fibrin entity? This study had three times as many "dry sockets" on the Papase[R] side as on the control side. Since there is very little information available on this aspect, more study is needed.

The author concludes that there is no pharmacologic substitute for skillful technique. Good surgical principles and techniques, with minimal trauma to the soft tissues, will minimize the severity of the physiological response, and create an optimal environment for healing. The overall feeling is that many questions must be answered and more objective studies performed before Papase[R] can be considered an acceptable and valued adjunct to surgical exodontia. This study will be continued, in an attempt to eventually provide a more meaningful addition to the literature.

(Abstract of report submitted during Postdoctoral Fellowship in Oral Surgery.)

The opinions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

DISTAL DISPLACEMENT OF THE MANDIBLE IN ADULT RHESUS MONKEYS

S. P. Ramfjord and J. J. Hiniker, J Prosth Dent 16(3):491–502, May–June 1966.

An investigation was conducted to observe clinically and to determine histologically the effects of a forced distal positioning of the mandible in adult rhesus monkeys. The distal displacement of the mandible was accomplished by means of cast gold splints cemented to the teeth. Splints were placed in both the mandibular and maxillary arches of each experimental animal so that the resultant forces directed the mandible distally.

Four adult rhesus monkeys were used and sacrificed at 2, 8, 16, and 35 week intervals. Necropsies and histologic studies of all organs were performed on each animal at the time of sacrifice. Also, block sections were obtained from the jaws and temporomandibular joints for histologic study.

Clinical observations showed that the monkeys were able to eat their full ration immediately after insertion of the splints. The animals either maintained their original weight or gained weight during the experimental period. The interdental space at full closure was measured at regular intervals. The teeth of the animals sacrificed at 2, 8, and 16 week intervals never made contact, but with time the space diminished. In the 35 week experimental animal functional contact of the posterior teeth was established at 20 weeks.

The histologic studies showed severe changes in the periodontal tissues and minor changes in the temporomandibular joints. The teeth moved bodily with the splints until posterior contact of the teeth occurred, at which time a slight distal displacement of the condyle had taken place.

In the 35 week animal, however, where posterior contact of the teeth occurred at the end of 20 weeks reversal changes in the temporomandibular joint were present. The condyles were being repositioned to their original position. This finding supported the concept of the dominance of the musculature in maintaining the position of the mandible.

The key findings of this study are:

1. Temporomandibular joints are resistant to dysfunctional changes of the occlusion.

2. Temporomandibular joint changes were temporary until adaptive changes in the repositioning of the teeth occurred.

3. Muscle balance was the most important factor in stabilization of jaw relationships.

(Abstracted by CAPT Perry C. Alexander, DC USN.)

TEMPERATURE CHANGES AND LOCAL ANESTHESIA

A. G. Westblade, Dent Abs 13(11):655, Nov 1968.

Maintaining the temperature of anesthetic solutions at body temperature is desirable to reduce discomfort at injection, to reduce postoperative complications, and possibly to increase the rate of onset of anesthesia.

Thermal variations in the order of 5°F could well be detected by the universal receptors in the oral tissues of subjects. Onset of anesthesia could be affected by heat, as thermal variations influence solubility, diffusion, the rate of chemical reactions, and surface tension.

Loss of heat in solutions reached 30°F in one minute where room temperatures were low. From the results it is obvious that the temperature of the heating medium must be in excess of body temperature to compensate for heat loss from removal of the cartridge from bath to injection.

(Westblade, A. G. 272 Allan Street, Kyrabram, Victoria, Australia 3620. Temperature changes and local anaesthesia. Aust Dent J 13:154–157, April 1968.)

PERSONNEL AND PROFESSIONAL NOTES

DOCTOR WATSON TO BE NEW EXECUTIVE DIRECTOR, AMERICAN DENTAL ASSOCIATION

Dr. C. Gordon Watson has been named executive director of the American Dental Association and will assume the top executive post of the 110,000-member organization on January 1, 1970.

Dr. Watson, who succeeds Dr. Harold Hillenbrand, was elected to the Chicago-based post at the ADA's 109th annual session in Miami Beach, Florida. Dr. Hillenbrand has held the post 22 years.

A resident of West Los Angeles, Dr. Watson served as ADA assistant secretary for four years prior to becoming executive director of the 5,300-member Southern California Dental Association in 1964.

Dr. Watson practiced dentistry in San Diego, California for 14 years and while there served as secretary of the San Diego County Dental Society, chairman of its Dental Health Committee, and on the SCDA Council on Dental Health.

He is a Fellow of the American College of Dentists and the International College of Dentists, as well as a Fellow of the American Public Health Assn. He is presently a Commander in the Naval Reserve and a member of the Board of Directors, Southern California Comprehensive Health Planning Assn. Other memberships include the American Society of Association Executives, Southern California Society of Association Executives and the Professional Convention Management Assn.

Dr. Watson, born in Rexburg, Idaho, is a graduate of Ricks College there; Brigham Young University, Provo, Utah; and Northwestern University Dental School. He also has studied at the University of Chicago's Graduate School of Business Administration and is a life member of the Xi Psi Phi Dental Fraternity.

CAPT NIIRANEN RECEIVES AWARD

CAPT Victor J. Niiranen, Pacific Fleet and Service Force Dental Officer, has been presented the Andrew J. Ackerman Memorial Award for his contributions to the rehabilitation of the maxillofacial patient who has been disfigured from cancer surgery or the acts of war.

The award presentation was made during the Sixteenth Annual Meeting of the American Academy of Maxillofacial Prosthetics in October 1968.

Doctor Niiranen has been active in this professional society since 1945, when the Navy pioneered the development of plastic artificial replacements for lost parts of the head and neck. This early research was conducted at the Dental School of the National Naval Medical Center, Bethesda, Md.

The award was given in memory of Dr. Ackerman, who pioneered in this field in the civilian professional community and contributed immeasurably to the total rehabilitation of the disfigured patient. Four award presentations have been made since 1961.

CAPT G. H. GREEN RECEIVES AWARD

The Chief of Naval Research has recently announced the presentation of an award to CAPT George H. Green, DC USN, for the development of a diagnostic test that accurately detects dental caries activity in its reversible, subclinical stages. The test is based on the observation that salivary samples from individuals with various degrees of dental caries activity exhibit highly significant differences in their ability to oxidize specific substrates. This discovery was first made by CAPT Green in 1957 while performing a series of salivary manometric studies with the Warburg Respirometer at the Naval Dental Research Facility, Great Lakes, Illinois.

While it was readily apparent that these findings could well serve as the basis for an extremely rapid and accurate test for dental caries activity, it would not be a practical test for routine use in the dental

office unless a method could be devised which did not require the use of expensive and complicated research equipment. After ten years of experimentation, CAPT Green has developed a practical method that enables the dentist or his assistant to make an accurate diagnosis of the patient's dental caries activity during a routine dental appointment. The test can be performed in a matter of minutes without the need of expensive equipment or special laboratory techniques.

Recognizing the potential value of a rapid and practical test for the diagnosis of dental caries activity in its incipient, preclinical stages, the Office of Naval Research has recently obtained the patent rights to CAPT Green's test for the Navy and the other Federal Dental Services.

JOINT PROFESSIONAL MEETING

The Fourth Force Dental Company, Force Troops, Fleet Marine Force, Atlantic, Camp Lejeune, North Carolina acted as hosts for a joint professional meeting held in November 1968. The meeting, held at the Paradise Point Officers' Club, Camp Lejeune, was a dinner affair with lecture following. Fifty dental officers from Marine Corps Base, Camp Lejeune; 2nd Marine Division, Camp Lejeune; 2nd Marine Aircraft Wing and Marine Corps Air Station, Cherry Point; Naval Hospital, Camp Lejeune and Marine Corps Air Station, New River were in attendance. In addition, eight civilian dentists from Jacksonville and Havelock, North Carolina were guests for the evening.

The clinician for the meeting was Dr. Clifford M. Sturdevant, Chairman of the Operative Dentistry Department, School of Dentistry, University of North Carolina, Chapel Hill, North Carolina. His subject was "The Cracked Tooth Syndrome: Its Diagnosis and Treatment."

ANNUAL MEETING OF THE AMERICAN STOMATOLOGICAL SOCIETY OF JAPAN

The 16th Annual Meeting of the American Stomatological Society of Japan was held concurrently with the 2nd Annual Meeting of the Far East Chapter of the Association of Military Surgeons in the fall of 1968. The joint meeting was held at Yokosuka, Japan. Both meetings, a tri-service effort, were hosted by the U.S. Navy. CAPT K. L. Longeway, DC USN, Force Dental Officer, COMNAVFORJAPAN, President of the Stomatological Society, welcomed over 100 Army, Navy, and Air Force dentists and over fifty distinguished Japanese dentists to the meeting. In his opening remarks, CAPT Longeway stated "The meeting was an opportunity to share our knowledge, promote mutual understanding and fellowship, and to participate in an interesting professional program." The meeting included two days of lectures, table clinics, commercial exhibits and displays.

NEWLY STANDARDIZED DENTAL ITEMS

The following newly standardized dental items are now available:

6520–086–6554	Preventive Dentistry Kit, Patient, Child, 36s:	PG	7.92
6520–935–1095	Wire, Steel, Corrosion Resisting, Threaded, 0.025 inch Diameter, 6 inch Length, 4s:	PG	1.81
6520–935–1096	Wire, Steel, Corrosion Resisting, Threaded, 0.022 inch Diameter, 6 inch Length, 4s:	PG	1.81
6520–935–1097	Drill, Pin Hole, Dental, Amalgam Reinforcement, 0.024 inch Diameter, 6s:	PG	3.21
6520–935–1098	Drill, Pin Hole, Dental, Amalgam Reinforcement, 0.027 inch Diameter, 6s:	PG	3.21

DENTAL EQUIPMENT SUPPORT PROGRAM

In order to expedite the resolution of any problems encountered in the shipment and procurement of spare parts or technical information pertaining to Ritter Company equipment, it is suggested that dental activities experiencing such difficulties contact the Federal Representative of the Ritter Equipment Company at the following address:

Ritter Company
400 West Avenue
Rochester, N. Y. 14611
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Dept of Defense Section

NURSE CORPS SECTION

INTENSIVE CARE UNIT

LCDR Laura L. Sowuleski, NC USNR, submitted this paper while attending a short course at the Naval Medical School, National Naval Medical Center, Bethesda, Maryland. She is assigned to the Naval Hospital, St. Albans, New York.

Intensive Care Units date back to 1863. Florence Nightingale organized a small room off the operating room to care for patients from surgery.

Patients' services have quadrupled since World War II. The growing feature introduced into the American hospital scene has been the Intensive Care Unit to supplement conventional nursing units for several types of patients. Now Intensive Care Units are an accreditation standard for large hospitals.

In the military hospital, a modified system of progressive care has been in effect for a considerable length of time. This has been brought about by the need for a patient to be ready to perform all or most of his duties before returning to his assignment. Thus, the maintenance of convalescent wards where little or no professional staff were required has long been the practice. Such wards provide dormitory accommodations and can be utilized for patients undergoing diagnostic studies as well as for convalescence.

In establishing an Intensive Therapy Unit, the plan was extended one step further by concentrating the more seriously ill in one site, where they could be cared for by a greater number of highly qualified professional personnel. In addition, expensive and necessary equipment was thus located in the unit. In this way, "dilution" of personnel and spreading, or duplication of equipment was minimized.

St. Albans Intensive Care Unit differs from other patient areas of the hospital in several ways. This area is a compact unit, an open ward with each bed position equipped with wall suction, oxygen outlet, wall sphygmomanometer, stethoscope, mobile intravenous pole and lamp. Mobile oral suction machine, intravenous tray, clip board with plotting sheets, intake and output, nursing notes and treatment sheets are included. All possible items such as drainage bottles, etc. are suspended beneath the bed. Positioning of equipment and contents of bedside locker is identical in each patient area. This facilitates location of needed articles in any emergency. Two single bed quiet rooms are used for isolation of infectious cases, i.e. pseudomonas. One section of the unit is used strictly for Open Heart patients. The bed capacity is 20 patients and the unit is completely air conditioned.

Flow of patients to the unit begins with the operative procedure or emergency admission. From the Operating Room they go to the Recovery Room, then by-pass the Intensive Therapy Unit and proceed directly to standard ward care. The acute emergency admission is directed to the Intensive Therapy Unit. From the Standard Ward they are transferred to the Convalescent Ward and discharged to duty or home.

Although greater use of the Intensive Care Unit is made by surgical services, the intent and design of the unit is utilized by the Medical Services as well.

Developed in the unit and an asset to efficiency during any emergency is the Emergency Cart. The Emergency Cart is complete with life-saving equipment—Ambu, intubation tubes, cardiac arrest tray, cardiac needles and knife. A Cardiac Monitor and Pacemaker and Defibrillator, Isolette respirator, air shields, adult and infant respirator, a Morch-Mueller respirator, and emergency drug box are also included.

Incorporated in the Nursing Procedures Manual are Intensive Care Unit routines, written in outline form in simple, concise language. Assigned members of each shift check all wall suction and oxygen outlets, oral suction machines, Emergency Cart and I.V. trays daily. Bedside units are restacked as used. Monthly cultures are taken from various areas on the ward. These reports are submitted to the officer in charge of Intensive Care Unit (Chief of Surgery).

Nursing care on the Intensive Care Unit is never a solo performance. A charge nurse assigned in this specialized area must be well versed in basic nursing skills, be an expert in giving medications and treatments and in observing patients for minute or gross responses, have a working knowledge of complicated or simple equipment, prevent infections, be able to delegate care of patients and make use of all spare time and slack periods to teach the ever-changing personnel.

An area on Intensive Care Unit which is a unit in itself is the Open Heart Surgical Unit. Located on the solarium of the Intensive Care Unit it is completely set up for all open heart surgical patients and staffed by a special team of nurses. Since particular empha-

sis on nursing diagnosis and decisions are extremely important in cardiac patient care a clinical instructor with specialized skills is assigned to teach the selected team of nurses. This highly skilled team is assigned the care of all open heart cases. These nurses must be able to determine the difference between cardiac failure and pulmonary failure, be skilled in resuscitation techniques, knowledgeable in reading monitors and experts in giving complex nursing care.

The nursing diagnosis and plan of care for each patient evolves from (1) a study of the patient's history and the doctor's goals and plans for treatment; (2) an understanding of the patient's health problem and the way in which it affects body and mind; (3) a tentative assumption about the patient's troubles and strengths in coping with them; and (4) evaluating the nursing care plan. This is accomplished by conferences, physical tour of the unit, full explanation of equipment and procedures to be done by the team selected to care for the patient.

Preoperatively the patient has extensive laboratory workup, x-rays and consultations. Preparing the patient ahead of time for all that he will experience and encouraging his expression of feelings are effective ways to prevent resignation. But even more important is helping the patient to use his own powers to gain control of himself and the situation.

Postoperative care includes x-rays, kilogram weight, monitoring equipment, intravenous fluids, blood transfusions, chest bottles, and oxygen therapy. Extensive doctor's orders include tracheostomy care, EKG, urine outputs, and measuring of chest drainage. The patient is moved to an open ward three or four days later depending upon his progress.

The primary purpose of comprehensive nursing care is the preservation of human life and the betterment of the health of each individual according to his particular needs. This is the accomplished goal on the Intensive Care Unit, Naval Hospital, St. Albans, New York.

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RESEARCH SECTION

LIST OF RECENT PUBLICATIONS FROM RESEARCH LABORATORIES

The following papers have been completed by research activities under the direction of the Bureau of Medicine and Surgery.

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"Applications of Biophysical Heat Transfer Studies in Protection Systems," by Alice M. Stoll and Maria A. Chianta. NADC-MR-6722, December 29, 1967.

"Effect of Physical and Psychic Stress on Phosphatidyl Glycerol and Related Phospholipids," by B. David Polis, Edith Polis, John deCani, H. P. Schwarz, and Lorraine Dreisbach. NADC-MR-6805, August 1, 1968.

"Pulmonary Hypertension Resulting from Oxygen Exposure," by George H. Kydd. NADC-MR-6802, June 5, 1968.

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OCCUPATIONAL MEDICINE SECTION

HOSPITAL SAFETY MANUAL

The American Hospital Association and the National Safety Council have jointly published a concise manual for hospital safety entitled the "Hospital Safety Manual." The Manual serves as a useful guide for the prevention of injury and occupational illness among hospital patients, staff, and visitors. The booklet includes such useful information as fire prevention, patient safety, special departmental problems and protecting the visitor from injury.

The "Hospital Safety Manual," a useful publication for all hospital departments, may be obtained from the National Safety Council, 425 N. Michigan Avenue, Chicago, Illinois 60611, as publication number 129. 55. Cost each: 1—$2.55; 2—$2.35; 10—$2.15

ASBESTOS BODIES AND BIOEFFECTS —A DETECTIVE STORY

John M. G. Davis, PhD, Great Britain; Robert T. P. deTreville, MD, Pittsburgh, Pa.; Paul Gross, MD, Pittsburgh, Pa.; Industr Hyg Found 32nd Ann Meeting Trans Bull No. 41, pp 81-84, 1967.

1. *Asbestos*—This is a general term that covers a number of fibrous minerals of which four types are of commercial importance. These are crocidolite or blue asbestos from South Africa; amosite which is red in color and is also mined chiefly in South Africa; chrysotile which is white and occurs in many countries of the world, and anthopholite which is also white and is mined mainly in Europe. The importance of this will become apparent when we discuss the finding of asbestos bodies in the lungs of the urban population in the North American continent.

2. *Asbestosis*—This is a type of lung fibrosis that occurs in workers exposed to large amounts of asbestos dust. It may or may not be associated with recognizable clinical disease during life, and is produced by all types of asbestos.

3. *Bronchial carcinoma*—This is the layman's lung cancer that we know is associated with heavy smoking and has also been found to occur frequently in workers exposed to large amounts of asbestos dust. Again, this tumor appears to be associated with all asbestos types.

4. *Mesothelioma*—This is a very rare tumor that develops from cells lining the chest and abdominal cavities. These tumors so far appear to be associated with exposure to only one type of asbestos, i.e., crocidolite which as has been noted is blue and is mined chiefly in South Africa.

Asbestosis was first recognized as an industrial disease at the turn of the century, but at the time, the bodies were not noticed. Later, in 1914, Fahr and Feigel discovered "strange crystals" in lung sections from a case of asbestosis. Later, Cooke in 1924, reported "curious bodies" from asbestosis cases, but because of their beaded structure, he thought they might be fungi. Stewart and Haddow in

1929 believed that the bodies were associated with the disease and coined the term asbestosis bodies and this term was used for some time until it became noticed that large numbers of bodies could be found in the lungs of asbestos workers without the presence of very much pathological change.

Gloyne in 1932 demonstrated that each body consisted of an asbestos fiber as a core with some coating material around it and it was suggested that this coating might have the function of protecting the tissues from the harmful effects of the mineral. This led to the term asbestos bodies being substituted for asbestosis bodies and there the situation remained until quite recently. The bodies, it was thought, only occurred in relation to asbestos and were regarded as diagnostic of exposure to this dust but not any real indication of disease.

This situation was only changed by the report of Wagner in 1960 that the rare pleural tumor, the "mesothelioma," was in South Africa associated with exposure to blue asbestos or crocidolite in the mining areas. The association of ordinary bronchial carcinomas with exposure to asbestos dust had long been recognized, but it has recently been shown that this is related to high dust dosages in asbestos workers and careful environmental control has almost eliminated this tumor as a problem in factories.

While asbestosis and bronchial carcinoma were obviously connected with severe dust exposure, these were solely problems for the asbestos industry; but if a very small amount of dust could cause a mesothelioma, might not asbestos products be a hazard to the whole population?

This asbestos scare has, however, ignored some of the published facts on mesotheliomas and new information suggests that others cannot be taken at their face value. First, asbestos is not a single mineral. Wagner reported quite distinctly that his mesothelioma cases were associated with the crocidolite areas and he found no cases associated with either amosite or chrysotile. In other countries attempts to demonstrate that exposure to dusts other than crocidolite could produce mesotheliomas have so far been almost completely unsuccessful. The mesothelioma problem is therefore not, as far as we can see at the moment, one that involves the whole asbestos industry, but only users of crocidolite and, fortunately, this mineral represents a relatively small proportion of total world asbestos consumption.

Asbestos bodies were for many years believed to be formed only around asbestos fibers, but recently evidence has accumulated that the deposition of a similar coating can occur around a number of materials, and studies have been undertaken in the Mellon Institute and in the United Kingdom in an endeavor to find out just how many materials will produce asbestos-like bodies, and also to attempt to discover the chemical processes involved. In order to discuss this work, it is necessary to summarize what is known about the structure and chemistry of genuine asbestos bodies.

Gloyne in 1932 had demonstrated that the body coating contained iron, and Berger in 1933 had shown that protein material was also involved. The presence of iron in the capsule has led to Perl's stain being used as an aid in finding these bodies. The capsule stains dense blue and is more easily seen in tissues than the natural brown color. When we first examined the structure of asbestos bodies in the electron microscope, we found that the coating was made up of small dense granules about 60 A° in diameter. Similar granules had previously been reported in a number of tissues and it had been assumed that they represented either ferritin or haemosiderin. Since this tied in well with the known iron protein nature of the capsule, it was suggested that the asbestos body coating was made up of one of these chemicals. As regards the anatomy of the bodies, it was found that although sometimes only one dense layer of coating material was present, in other cases the coating consisted of a number of different layers of varying thickness and density. Occasionally the outermost layer was made up not of granules but fine filaments about 60 A° in diameter which we now believe to represent calcium deposits.

For the experimental production of bodies with non-asbestos materials, two techniques were used. In Pittsburgh, hamsters were injected intratracheally with the dust, while in Cambridge we used intrapleural injection. The dusts used were aluminum silicate, glass fiber, carborundum, man-made textile fiber and elastin. In both injection sites all these foreign materials produced bodies which with the light microscope appeared very similar to asbestos bodies. That is to say they were golden brown in unstained sections and were often segmented. Perl's stain showed that the coating contained iron in common with asbestos bodies. For this reason Doctor Paul Gross in Pittsburgh suggested the term "ferruginous" body and suggested that this general term should be used for all bodies found in human lungs at least until the mineral involved was positively identified.

The situation at present is then that one must not assume that "ferruginous" bodies seen in the lungs of the normal population are asbestos bodies until their mineral core has been definitely recognized. Almost the only method of identifying these small particles accurately is by electron diffraction and this involves a very great deal of work in manipulating the small bodies onto an electron microscope grid. However, in Doctor Gross' laboratory, a study of these structures has commenced which we hope will give an indication of what percentage of human "ferruginous" bodies are caused by asbestos.

Summary

Asbestos has been related to certain bioeffects which appear specific and are dose related. These effects include asbestosis which will occur in almost all exposed persons if sufficiently high exposures are maintained for long enough periods. In addition, some individuals so exposed develop bronchial carcinomas. Industrial hygiene practices have been very effective in controlling both these forms of occupational disease.

There has been recognition for many years that workers exposed to asbestos dust develop "asbestos bodies." First observed in individuals who had asbestosis they were called "asbestosis bodies" but when it became evident that they frequently occurred in the absence of this disease, the name was changed to asbestos bodies.

The current furor over asbestos bodies results from two developments which recently appeared in the professional literature and news media. This has resulted in considerable public apprehension on an international scale. These developments were: firstly, Wagner's study of mesothelioma cases associated with crocidolite asbestos exposure often non-occupational in nature, and secondly, Thompson's conclusions that asbestos is a significant urban air pollutant based on his findings that over 26 percent of urban dwellers can be shown to have asbestos-like bodies in their lungs.

Because of this, some individuals have expressed the opinion that asbestos should be withdrawn from many of its uses, e.g., in brake linings. However, the basic assumption that asbestos-like bodies can only be produced from asbestos has proved incorrect and this casts considerable doubt on the theory that has been the chief basis of the asbestos "scare."

GET OFF MY BACK

Robert N. Hart, San Diego, Calif., National Safety News 98(5):62–66, Nov 1968.

One of the most popular activities in safety work is the constant advocacy, demonstration, and promotion of "the proper way of lifting."

It seems to be almost universally agreed that this prescribed method is the major means of preventing back "injuries," which are so numerous in almost any kind of work.

It is my contention that only a small portion of the many reported back "injuries" are even potentially susceptible to this method, and that none actually are.

Another fact that I have found extremely disturbing throughout years of safety work is the very high percentage of back conditions reported and accepted as "injuries."

It is proposed that all of us in the field of safety take a long, careful look at our orthodox views on alleged back injuries. We might then be able to turn more of our attention to the prevention of real back and other injuries.

An Examination

In almost every instance where an employee develops a back condition while working or during working hours, it is reported as an injury—and is presumed to be the result of an accident. As such, they constitute a high percentage of all injuries—from about ¼ to ⅓ in our organization.

Over a period of years, many reports of injuries to the backs of employees that were attributed to their work, or incurred while they were at work, have been studied.

A remarkable variety of back conditions and ailments exist—ranging from "whiplash" to a fractured coccyx. Involved may be muscles, tendons, ligaments, discs, vertebrae, or nerves—and often the doctor doesn't know which.

A study was once made of more than 200 cases of back conditions reported over a period of three or four years—most of which supposedly resulted from "strain" or the physical efforts of the individual himself. The following percentages are only approximate as they varied in different periods.

The remarkable fact is that about 20 percent involved no strain or effort of any kind other than that required simply to move; not suddenly, violently, or with any other kind of difficulty.

Another 65 percent were incurred while engaged in what could be described only as moderate or mild physical efforts. About 10 percent were doing "heavy" or "strenuous" work, little if any of which could be considered excessive or unreasonable. In only four or five percent of the cases was straight lifting alone being done.

Observations

As a result of these studies coupled with discussion, experience, knowledge, and reasoning, there are a number of things that seem to be strongly indicated:

1. The first and foremost: in every case not involving an externally imposed force, the condition in the back is only coincidental to whatever circumstances attended its manifestation.

2. In most cases, there simply can't be an excess of stress on any part of the back. I believe that there existed some kind of predisposition or physiological susceptibility, which happened to manifest itself at a particular time.

3. Conversely, I contend that no one can have any of these conditions occur solely as the direct result of any amount of self-imposed strain. By self-imposed is meant imposed by the sheer muscle power of the individual himself. This does not include strains resulting from falls, blows, and suddenly or externally applied force.

As these assertions will undoubtedly be received with considerable doubt and perhaps little acceptance, explanation is certainly in order. These conclusions have been arrived at after years of personal experience with all kinds of physical effort. Efforts and activities of others have been carefully observed also. This background—coupled with some knowledge of the human structure and physiological facts and a study of circumstances and medical diagnoses —have led to these conclusions.

More Observations

Other factors seem evident from the studies made. These seem to warrant fairly firm tentative conclusions, which can be used until more scientific data is available.

It does not appear that age is correlated with the incidence of back injury. Many younger people, such as police and firemen, seem to be frequently involved. On the other hand, many older employees, regularly doing heavy and strenuous physical labor, do not appear to have any more such trouble than younger people.

There is little or no indication that the amount of weight being handled has any bearing on the incidence of back ailments. A very high proportion of all cases reported involve only moderate weights or none at all. There are many reports of feeling a sudden stab of pain in the lumbar region while simply bending over or reaching. On the other side of the coin is the fact that there are many who lift 200 pounds or more without difficulty.

It seems futile to attempt to establish limits as to the amount of weight that may be handled—supposedly with safety. In most instances, such as with trash containers, there is no practical way to determine the weight before handling.

The form of the weight—i.e., a pound of lead or a pound of feathers—is another significant factor. Any selection of a weight limit is necessarily arbitrary. Every individual has a different capacity as to what he can handle with or without regard to doing so safely.

We have seen little correlation between the nature of the work being done and the development of back conditions.

It often seems that there are more instances of back trouble in those who perform sedentary or light work. Perhaps there is an inverse relationship, if enough statistical evidence were available.

There may be a number of times when working conditions involving heavy effort and strain may bring out a condition from a predisposition or susceptibility such as discogenic disease or bone spurs. Some of the more serious cases appear to be in that category.

One factor we have not been able to observe is whether those who have not been doing heavy physical work—either recently or ever—are more susceptible to back trouble soon after engaging in it than those who are doing heavy work regularly. It is a fact that muscular soreness in all muscles being used almost always develops after unusual and strenuous efforts.

Proper Method of Lifting?

It appears to me that the main premise of the recommended method of lifting is that most back injuries are the result of overstressing certain elements of the back—muscles, tendons, ligaments, and perhaps discs. Yet it is evident that there could not have been excessive stress on any element. As said before, often there is no stress except that required for movement. Sometimes pain and a disabling condition develop some time after the circumstances to

which they are attributed. Often the attending circumstances cannot in any sense be regarded as an "accident" or a "cause" of the condition—and in many other situations, there is substantial doubt of any cause and effect relationship.

It is my opinion that this theory of the cause of back injuries is medically and mechanically fallacious. Though I am not a physician, I do have some medical and physiological knowledge. I am a mechanical engineer, and do not agree with the mechanical analogy of the cause of backstrain.

Not only is the real nature and cause of many ailments in doubt, so is the cure. Heat and rest appear to be the best treatment. Some conditions clear up in a day, while others appear to linger for some time. Some become chronic and seem to indicate a continuing cause other than the effects of a strain that would be expected to heal sooner or later.

Considerations

There are several facts that should be considered in regard to the recommended method for lifting safely. Relatively few jobs involve just straight lifting. Most jobs requiring physical effort necessarily involve compound body action in which lifting, bending, twisting, and turning are all needed to accomplish the necessary results.

To whatever extent the recommended method is natural and comfortable to the individual—it will probably be done anyway. Some prefer using the legs, but perhaps more use the back.

Conversely, if the recommended method is felt to be awkward and inconvenient, it is not likely to be used. At any rate, both the back and the legs are inevitably involved to some extent in lifting—under any circumstances.

If the load is held in front of the body (as it must be if the back is to be kept vertical) the arms will necessarily be at an angle to the spine. The load will then apply a torque through the arms to the back. This amounts to the same stress as when the arms are vertical and the back is at an angle.

Of course, the amount of the angle can vary, but the individual is likely to choose the method that is easiest and most comfortable for him—particularly if he is doing it repetitively.

From the standpoint of economics and individual productivity, the time element is a serious consideration. It is unlikely that any method that is artificial, unnatural, slow, and inefficient will be employed.

It can be argued that the loss from back injuries may offset the economy of the speed and efficiency of an "improper" method of lifting. This could be true so again I return to my contention that back injuries are not caused by improper lifting.

Other Considerations

Some things have been observed that indicate certain possibilities.

Many reports state that the victim (with or without a burden) had a sudden slip, twist, trip, or loss of balance at the time of a pain in the back. Sudden efforts of various kinds have been described in connection with not only back strains but other injuries as well.

Probably, more often than not, these things do not result in a serious condition. But it is a valuable part of every safety program to urge the avoidance of slips, trips, and unnecessarily sudden movements of any kind that can lead to a variety of accidents and injuries.

One generally accepted principle in sports involving heavy sustained effort is the warm-up. True, many athletes have suffered serious strains even after warming up and extensive activity.

Nevertheless, warming up seems to be a beneficial policy, which probably minimizes the incidence of muscular ailments during strenuous efforts. That is undoubtedly true when any predisposition or susceptibility exists.

Several other factors may influence the individual's suspectibility to back troubles. One seems to be heavy use of alcohol; another a considerably overweight and somewhat flabby condition. Fatigue is another factor that may contribute to susceptibility. It should be combated in safety programs as it is a potential cause of many accidents.

Classification of Back Cases

If the individual sees a physician, the latter should be informed of the supposed circumstances. The diagnosis should be studied, particularly if x-rays were taken. The diagnosis will either clearly show an actual injury or merely reiterate the patient's report of pain.

Information to be gathered and considered include:

1. Actions and the type of effort involved
2. Tools, equipment, materials involved
3. Weights and degree of effort involved
4. Surrounding circumstances and their severity
5. Would the circumstances reasonably be expected to cause an injury to any one
6. Is there any evidence of any predisposition to that type of injury (e.g., a previous injury)
7. Medical diagnosis.

SEQUELAE OF POISONING FROM PHOSPHATE ESTER PESTICIDES

Irma West, MD, Berkeley, Calif., Industr Med Surg 37(11):832–836, Nov 1968.

The first death from a phosphate ester pesticide occurred in California in 1949 when a sprayer at a University of California Agricultural Experimental Station mixed and applied parathion all day using no precautions. Two other deaths occurred about the same time in other states during the first applications of parathion. Since then, 33 accidental deaths and over 2,800 cases of nonfatal occupational poisoning from parathion and other phosphate ester pesticides are on record in California, 1953-1966. There is no reporting system for nonoccupational poisoning so the number which may have occurred among the general public is unknown. The reports of occupational poisonings provided only information about the acute episode. If any sequelae were subsequently noted they were not placed on record.

There has been just one study following up California workers who were poisoned by phosphate ester pesticides to determine the incidence and kinds of sequelae. This study reported upon 114 workers who were located and examined three years after their poisoning episode. Forty-three had complaints for six months, and thirty-three still had complaints primarily in these categories: optic, gastrointestinal, cephalic, cardiorespiratory, and neuropsychiatric. Included was a significant number who were intolerant to further pesticide exposures. It was concluded that this study would have detected serious aftereffects of high incidence, but not those which were minor, those which followed only very serious poisoning, those from exposure to specific compounds, and those occurring only in hypersensitive individuals or under other unusual circumstances.

From a study of workers in Colorado comes a report that "many" complained of persistent symptoms a year after an acute phosphate ester poisoning episode. These symptoms included fatigue, irritability, visual problems, slowed mental processes and a variety of aches and pains.

Three out of ten young workers who experienced organophosphorous poisoning in Russia were affected for 2-4 years with an "asthenovegetative syndrome" which reduced their work capacity. General weakness, fatigue, insomnia, and increased perspiration were among their complaints.

Neurological Sequelae

Human cases of delayed, persistent or permanent nerve damage have been reported following acute poisoning from parathion, EPN (Ethyl p-nitrophenyl thionobenzene phosphonate), malathion, and Mipafox (bismonoisoproply-aminofluorophosphine oxide). TOCP (triorthocresyl phosphate), which is a phosphate but not a pesticide, has been cited as the cause of a number of cases of peripheral nerve damage among persons accidentally ingesting it or occupationally exposed to it.

There is some difference among investigators regarding the nature of the neurological pathology produced by these organophosphorus compounds. In chickens it was observed that axon degeneration of the long nerve fibers, similar to that occurring in nutritional deficiency, was the basic lesion rather than demyelinization, which was secondary.

EEG (electroencephalogram) abnormalities have been reported following human poisoning.

Psychiatric Sequelae

In 1961, sixteen cases where Australian workers were chronically exposed to various phosphate esters and subsequently developed either schizophrenic or depressive reactions were reported. These reactions persisted as long as six months after exposure ceased but reverted to normal in twelve months.

In 1963, two cases of psychiatric symptoms developing in agricultural aircraft pilots with a long history of repeated exposures and episodes of poisoning from organophosphate poisoning were described. Symptoms persisted long after exposure had ceased but with eventual recovery. One was hospitalized for a depressive reaction. The other experienced recurring episodes of acute anxiety.

In 1965, an epidemiological study carried out in Australia attempted to find if the incidence of males hospitalized for psychiatric disorders was higher in geographical areas where organophosphorus compounds were used. They found no such relationship.

Experimental studies with one phosphate ester compound (diisopropyl-fluorophosphonate) indicated that when the dose is sufficient, psychiatric illness can be aggravated and mental symptoms can be induced in normal persons. The changes persisted for several months after withdrawing the compound.

Psychological and Functional Sequelae

Tests for mental alertness were carried out on groups of workers with various kinds and degrees of exposure to various phosphate ester pesticides and on control groups. Only when the subjects were exposed sufficiently to cause clinical illness was there

a significant difference between the exposed and the control groups.

Another series of patients were tested at varying intervals during and after acute poisoning. The greatest disturbances occurred among the most severely affected at times closest to the onset of symptoms. The poorest performance was among those who had experienced previous exposures and was inferior to that of the controls even some time after the last exposure.

In this same study the persistent effects observed following poisoning included fatigue, irritability, forgetfulness, nervousness, and carelessness. Fellow workers and foremen evaluated workers who had one or more episodes of poisoning. Sixty-eight to 75% were believed to show adverse changes in work performance and 64-70% showed changes for the worse in their behavior.

Hematologic Sequelae

Disturbances in blood coagulability were noted in the majority of 31 patients poisoned either with parathion or nerve gas. In ten cases, hypocoagulability was observed with shortening of prothrombin time or an increase in thromboplastin activity. Hypocoagulability was noted in fifteen cases with prolonged prothrombin time. In 35% of these cases fibrinolysis was present.

Among the more than 1,000 cases of phosphate ester poisoning, there were only a few observed whose sequelae could have been related to disturbances in coagulability. One developed a thrombophlebitis, two had probable coronary thrombosis, and three had hematuria.

Four out of eleven Korean cases of acute parathion poisoning had microscopic hematuria.

Leukocytosis has been noted in a number of cases of acute phosphate ester poisoning.

A study of several hundred Canadian apple growers exposed to pesticides showed a greater incidence of leukopenia and neurological abnormalities than controls. However, the subjects used chlorinated hydrocarbon, and phosphate ester pesticides as well as mercury and other pesticides.

Renal Sequelae

In the process of following a group of Florida workers using parathion, it was discovered that one of them unlike the others was not excreting PNP (paranitrophenol), a metabolic end product of parathion. He had been receiving regular and excessive exposure for some time. It was determined that he was not excreting PNP because his kidney function was impaired. PNP is a toxic chemical about which there is inadequate toxicological information. Its effects are reported to be similar to phenol and aniline poisoning.

Evidence of renal tubular dysfunction has been reported in 15% of twenty-eight workers occupationally exposed to parathion, and in two of six acutely poisoned workers. Decreased phosphorus absorption or impaired hydrogen ion secretion or glycosuria were observed.

Glycosuria and proteinuria has been reported in routine urine tests of victims of phosphate ester poisoning.

Whether these abnormalities in renal function persist to the point where they could be categorized as sequelae or lead to sequelae has not been subjected to sufficient study.

Accidents

Accidents may follow poisoning or occur while persons are poisoned from phosphate ester pesticides. Of 232 cases of phosphate ester poisoning followed three years later in California, four had died. One died of a subsequent episode of phosphate poisoning and three died in motor vehicle accidents. Of these, two were driving home from work after working all day with phosphates.

In six fatal agricultural aircraft accidents investigated in California, 1967-68, two showed a significant reduction of red cell cholinesterase. Neither were applying phosphate ester pesticides at the time of their death, but had received exposure during the preceding few days. Their planes hit objects which the pilots should have been able to avoid.

Sequelae Related to Treatment

Theoretically, the large doses of atropine used in treatment of acute poisoning could precipitate acute glaucoma in susceptible individuals. No such case has been reported in the literature available to us. However, victims of phosphate poisoning are most often younger than persons most subject to glaucoma. Atropine is also capable of producing bizarre, mental and neurological symptoms as well as hyperthermia, but no such manifestations attributed to atropine used in the treatment of phosphate poisoning have come to our attention.

Certain drugs are contra-indicated in treatment of phosphate ester poisoning. Phenothiazine tranquilizers for example can increase the severity of symp-

toms of poisoning. Insufficient observations have been made to determine if unexpected sequelae could arise among persons who were taking tranquilizers at the time they were exposed to phosphate ester pesticides.

Brain Damage From Anoxia

One of the most serious sequelae of prolonged unconsciousness which may occur in many kinds of poisoning, including phosphate ester poisoning, is brain damage from anoxia. Only one such case of poisoning in a child, which subsequently died, is on record in California. Three cases were reported elsewhere who also died one to four weeks later.

Comment

The literature on potential, suspected, and established sequelae of phosphate ester poisoning does not confirm the often repeated statement that clinical recovery from nonfatal poisoning is always complete in a few days. On the other hand, no easily recognized, serious or permanent sequelae have been sufficiently frequent to make themselves obvious.

Somewhere between the two extremes, there are a variety of suspected or actual sequelae which may occur in a sizeable minority of cases. A sampling of these sequelae have been collected and reported upon in this paper. Some of these aftereffects may, in the light of future evidence, prove to be connected to poisoning in a purely circumstantial way. Others may actually occur more frequently than now recognized because the connection was unsuspected.

ENVIRONMENTAL HEALTH PROBLEMS IN INSTITUTIONS OF HIGHER EDUCATION

Irving R. Tabershaw, MD, Berkeley, Calif., Samuel I. Fuenning, MD, Lincoln, Nebraska, J Occup Med 10(11):663–666, Nov 1968.

Disease or danger is rarely associated with the conventional scene of a teacher lecturing to a class or writing on a blackboard. The sedentary activities of study and learning would be classified as the safest activity that one can choose. Modern institutions of higher education, however, are complex and stressful environments which arise from the massing of students and faculty in a limited area. Also, serious hazards may originate in some phases of the learning process, particularly scientific research. Similar principles and needs underlied the practice of occupational medicine in such diverse industries as a steel mill, a tannery, a bank, a mine, an oil refinery, or a public utility.

Environmental Conditions

The range of environmental health problems on a major campus is more like that of a military base or an oil refinery in a foreign country than that of a local industry. This tremendous range of problems can be classified as conventional, which embraces: (a) pollution—water, air, solid; (b) physical safety —fire, traffic, explosion, athletics; (c) sanitation—housing, food services, swimming pools; (d) environmental—light, noise, ventilation. These are not different from those encountered in any community. In military establishments, a rigid structure with clearly defined authority and responsibility is normally in charge of control of these problems. The essential difference on the campus is that the responsibility of the institution is normally vaguely defined, often conflicts with local jurisdictions, and usually receives little or no attention until disaster strikes. The special hazards further differentiate campus communities from industry and cities. These may be grouped as (a) biological—animals, infectious micro-organisms; (b) physical—ionizing radiations, lasers; and (c) chemical—carcinogens, toxicants.

Most of the special hazards arise in connection with research projects. These problems are characteristically short-term and indefinable because research is essentially a batch process dealing with unknown potentials for injury and illness. Exotic chemicals, unusual combinations, mutagens and carcinogens on which there is no background of toxicologic information are normally used for experimental purposes. Graduate students engaged in these pursuits have little concept and usually no training in recognizing the potential dangers. Nor are they particularly interested because there is no academic constraint to force the issue. Many of the operations are not repeated, and there is little chance for education during the course of an investigation.

Biologic laboratories present a type of hazard which occurs in some industries but is not very common. Unusual zoonoses, e.g., equine encephalitis and psittacosis, are constant threats in one laboratory. Viruses, e.g., leukemic virus known to be transferrable in animals, are handled by many without our knowing whether there is potential danger of transfer to man. The hazards inherent in ionizing radiation and lasers may be well known, but these aspects are rarely discussed with students who are not well informed of the potential for harm. It might be illustrative to enumerate a few problems recently encountered on our campus—the mixing of hydrogen

and oxygen in stoichiometric amounts and ignited to study the explosion patterns; field trips under hazardous conditions by untrained people to collect poisonous reptiles; scuba diving in dangerous waters; sanitation problems in a high altitude research station where temperatures are below freezing; nitrocellulose dissolved in acetone as an embedding fluid, a two-story electron microscope with a Freon atmosphere capable of asphyxiating the operators; a fog chamber for testing airplane instrument approaches and for dispelling fog; an experimental theater where new stage techniques are being tried. Problems of this kind add spice to the work of the environmentalist and test the best professional skills.

Editor's Note: Some may question the applicability of this article to Navy occupational health but the questions raised by Doctor Tabershaw concerning environmental problems in research laboratories have obvious parallels in naval laboratories.

PRACTICAL USE OF STRESS TESTING IN INDUSTRY

Richard W. Call, MD, Basil Clyman, MD, and Don R. Kaserman, MD, J Occup Med 10(11):649–654, Nov 1968.

The increasing number of supposedly healthy young men afflicted with heart disease each year has caused major concern in industrial management as well as medical circles.

Accordingly, in the past several years clinicians and physiologists alike have intensified their efforts to characterize the biochemical and electro-physiological events occurring in the potentially diseased heart. In most instances, their studies have dealt with the electrocardiographic response of the human heart under conditions of exercise stress. Thus have evolved the various cardiac stress tests, beginning with those of Selig, Rappoport and Wilson, and culminating with that of Master, namely, the double two-step.

Numerous investigators such as Bellet, Mattingly, Dimond, Doan and others have presented their respective series attesting to the feasibility of the procedure as a means of detecting and even quantitating preclinical heart disease. Some workers, like Bellet, have modified Master's double two-step procedure by introducing the treadmill or bicycle ergometer in order to evoke a more graduated exercise effort. The recent addition of radiotelemetry permitting the uninterrupted monitoring of the electrocardiogram throughout the procedure is still another refinement of this method of stress testing.

A radiotelemetry exercise test has been used as a means of detecting asymptomatic heart disease amongst management personnel. But for certain exceptions, noted later, this procedure is currently performed as a regular part of the annual physical examination available to members of the Union Oil management in Los Angeles. Our sample was composed of young to late middle-age Caucasian males, who for the most part were college graduates. This communication describes the mechanics of the procedure and to review the electrocardiographic data in the light of criteria proposed by Master and others.

The information at hand will be extended by the completion of a long-range prospective study to render more definite impressions concerning the procedure's predictive value for uncovering heart disease.

Procedure

Subjects with any history or clinical evidence of heart disease were excluded from this study. Also excluded were those unable for reasons of fatigue, muscle cramp, dyspnea, etc., to complete the exercise phase. Finally, we omitted from this study all patients taking medications such as digitalis, quinidine or anti-anginal preparations. The test was conducted on 396 subjects. They were instructed to refrain from all smoking and food intake for ten hours prior to procedure time, usually the overnight period.

Three pieces of equipment were required for this procedure. The treadmill employed was a compact office-type unit with fixed ten percent incline and adjustable speeds up to five miles per hour. A commercially available radio electrocardiographic system, which includes a light-weight transmitter and table top receiver, and a conventional office electrocardiographic recorder were used to monitor the patients.

With the patient recumbent, a standard resting 12 lead electrocardiogram was obtained. A physician in attendance reviewed the tracing and if it was normal, the patient was permitted to proceed to the exercise phase.

Baseline electrocardiogram strips were obtained with the patient in the standing position. Just prior to ascending the treadmill, the patient was briefed on the rationale of the procedure and instructed to express immediately any complaints of fatigue, leg cramps, chest pain, dyspnea or other discomfort.

The patient was started at 1.7 miles per hour and continued for two minutes. The speed was then

increased to three miles per hour for one minute, and then raised to four miles per hour for another minute and finally to five miles per hour for the concluding minute. Throughout the entire five minute exercise period the electrocardiogram pattern was constantly monitored by the physician in attendance. The occurrence of frequent premature ventricular contractions or a tachycardia of greater than 160 beats per minute was sufficient reason to terminate the treadmill exercise.

Immediately upon dismounting the treadmill the patient resumed a recumbent position and at one minute intervals for the next ten minutes, electrocardiogram tracings were obtained. If, at the end of ten minutes the pre-exercise resting pattern and rate had returned, the test was concluded. If not, further serial electrocardiogram strips were taken each minute until the initial pattern reappeared. This was rarely in excess of 15 minutes.

Results

The tracings obtained during the following exercise were analyzed. A tachycardia of over 160 was felt to be indicative of poor physical conditioning rather than actual coronary artery disease. J-point depression of less than 3 mm was not considered significant.

Of the subjects tested, 13.6% had positive tracings on the basis of one millimeter or more depression of the ST segment; 9.1% of the subjects had positive tracings because of a QX/QT ratio to greater than 50%; and, 14.7% of the subjects had equivocal tracings because of a J-point depression in excess of three millimeters.

Discussion

Occupational medicine has yet to fully exercise its full capability in the area of cardiovascular disease detection. This entity is the largest single cause of mortality in the United States today. Our major difficulty thus far has been our inability to diagnose latent heart disease early enough to effectively implement the appropriate control measures relating to weight, diet, lipid metabolism and exercise. The occupational physician who is medically responsible for large numbers of people should be in the forefront of this program. It should be one of his basic responsibilities to detect the disease process as early as possible and expedite the remedial measures necessary. A negative or passive attitude is no longer acceptable.

In the diagnosis of silent coronary artery disease, history and physical examinations are unrewarding and the resting electrocardiogram has been of little or no assistance. Even in the face of angina pectoris the resting electrocardiogram is normal in at least 50 to 83% of the cases. Development of stress testing by Master and his group has greatly broadened the diagnostic usefulness of the electrocardiogram.

Initially in our work with the stress test we utilized only the double two-step method of Master, where the energy demand is equal to six times, the basal requirement. Though relatively successful in our detection of certain unsuspected cases we, like other observers, were troubled by the significant number of false negatives. We felt that this could in part be remedied by using a system such as Bellet's that evoked more myocardial stress. As a result our test group of 396 men was started at 1.7 miles per hour on a ten percent grade, which is equal to four times resting basal, and gradually increased. At three miles per hour the energy requirements were five to six times resting basal, or the equivalent of a Double Master Two-Step. At four miles per hour the subjects were between seven to eight times resting basal. At five miles per hour they were ten to 12 times resting basal. Resting basal is equivalent to 1.4 Calories per minute.

This represented a submaximal effort for most of the men involved. Although they were largely a sedentary group, with a majority between age 40 and 60, almost all completed the five minutes without undue strain. We had exercised an earlier group to maximum effort, but abandoned this for fear of provoking morbidity in those unused to exercise. There was one patient who developed a brief run of ventricular tachycardia without any preceding premature ventricular contractions, but this subsided spontaneously within one minute following cessation of exercise. There were no further complications with this patient.

A depression and straightening of the ST segment of at least one millimeter with or without a terminal dip, was for use the only electrocardiographic alteration that signified definite myocardial ischemia. The ST segments that were not completely horizontal or sloped upward were designated as non-diagnostic. As expected, the more obvious or significant electrocardiographic changes began to appear during the fourth and fifth minutes. In some the typical ischemic

Dr. Call is Medical Director; Dr. Kaserman is Assistant Medical Director; and Dr. Clyman is Consultant, Union Oil Company of California, Los Angeles, Calif. (P.O. Box 7600) (Zip Code 90054)
Reprint requests to Dr. Call, Union Oil Company of California, Los Angeles, Calif.

pattern occurred only after three or four minutes post-exercise and remained present for five to ten minutes thereafter. These same patients during exercise demonstrated only minimal J-point depression. Thus, unequivocal evidence of myocardial ischemia was found in 13.6% of the 396 subjects tested. There were no positive tracings found in the 20-year age group. However, in the 30- and 40-age group there was approximately a five percent positive return. Predictably the older age group yielded the highest percentage of positives. This was particularly evident in the group age 45 to 50, where 15% returned a definitely positive record. In the group age 50 to 60, the percentage jumped dramatically to almost 29% and by the early 60's it was approximately 55%. These findings are consistent with the known clinical pattern of coronary artery disease appearing as early as the fourth decade, and progressing sharply over the next 20 years.

Master and his group have suggested that a QX/QT ratio greater than 50% is diagnostic. We have separated out those patients with only this finding. We will proceed to follow this group to determine if their incidence of overt coronary artery disease is indeed any greater than that found in normal controls. The age distribution of those having a prolonged QX/QT ratio was quite similar to that described for the group having abnormal ST segment depression.

The importance of developing a technique to diagnose early coronary disease in a large population has been stressed. Such must be accurate, economical and safe for the patient. The method herein described appears to satisfy most of the specifications cited. By constant electrocardiographic monitoring during exercise one may have advanced warning of possible complications and hence terminate this phase in time. Also, transient ischemic changes may be detected on the continuous record that would otherwise be missed using post-exercise observations alone. It has the advantage of stressing the heart at a very low level in the early stages and then gradually increasing the work load to a maximum of ten to 12 times resting basal. In our experience this has been done without undue risk.

As yet complete criteria have not been developed. The ST segment straightening and depression of one millimeter or more has been accepted by us as representing definite myocardial ischemia. Most and Hornsten *et al.*, in their recent publication, have also upheld the value of this criteria. In our laboratory, when this test was performed by young asymptomatic adults (ages 18 to 22 years) exerting maximal effort, the only electrocardiographic response apart from sinus tachycardia (160–180 beats per minute) was a J-point depression up to one millimeter. ST segment depression was never observed and the QX/QT ratio never exceeded 50%. We intend to follow this group of 396 men for the next five years and hopefully determine the outcome of the various classifications.

Conclusion

A technique has been described which will allow the occupational physician to evaluate a large number of employees for unsuspected or latent coronary artery disease. It has the advantage of ease of application, safety and apparently a high degree of accuracy.

In this study of 396 men at management level, aged 26 to 64, there was an over-all 13.6% positive electrocardiographic finding of asymptomatic coronary artery disease. This incidence of positive tracings increased markedly with advancing age. No serious, untoward reactions were experienced. With this prospective study of 396 employees we hope to further refine this technique and possibly establish more precise electrocardiographic criteria.

(The figures and references may be seen in the original article.)

EDITOR'S SECTION

NEW AND OLD DRUGS FOR PARKINSONISM

As a result of studies of biogenic amines in the brains of patients with idiopathic and postencephalitic parkinsonism, a major advance in the treatment of symptoms of this disorder appears to have been achieved. Clinical investigations under way for as long as two years in several American research centers show that oral administration of large doses of the amino acid L-dopa (levodihydroxyphenylalanine) can relieve many of the disabling symptoms of parkinsonism, including akinesia, rigidity, and to

a lesser extent, tremor. Some patients have experienced little benefit; generally, however, use of the drug has resulted in substantial and occasionally complete relief of symptoms. Up to the present time, most of the patients in the trials have been taking the drug for many months, a few for as long as two years. L-dopa is still in the investigational stage, and its use is limited to the few research centers where continuing studies are in progress.

Early Studies of L-dopa—The clinical studies followed the observation that dopamine (dihydroxyphenethylamine or hydroxytyramine), a catecholamine and a precursor of norepinephrine, was concentrated chiefly in the basal ganglia and that there was a marked depletion of dopamine in the basal ganglia of patients with Parkinson's disease (H. Ehringer and O. Hornykiewicz, Klin. Wschr., 38:1236, 1960). To administer dopamine was the next logical step, but it does not cross the blood-brain barrier; however, dopa—the immediate precursor of dopamine—does, and in a clinical study, intravenous administration of L-dopa provided some relief of parkinsonian symptoms (W. Birkmayer and O. Hornykiewicz, Wien. Klin. Wschr., 73:787, 1961). In subsequent years, most studies with L-dopa, the pharmacologically active isomer of DL-dopa, usually administered intravenously and in small doses, showed favorable but not remarkable or consistent effects.

Effectiveness of L-dopa—G. C. Cotzias et al. were the first to demonstrate the effectiveness of large oral doses of L-dopa in relieving parkinsonism (New Eng. J. Med., 276:374, 1967; presentation to the American Academy of Neurology, Chicago, April 1968; and the Association of American Physicians, Atlantic City, May 1968). The degree of improvement in 26 patients given L-dopa orally in dosages of 4 to 8 Gm daily ranged from modest to dramatic. The major adverse effects noted in this study were transitory nausea and vomiting in many patients, orthostatic faintness in some, and transient depression of granulocytes in a few. Ten of the 26 patients showed reversible, dose-dependent abnormal head movements.

These findings have been generally confirmed in a controlled study by M. D. Yahr et al. (presented to the American Neurological Association, Washington, D.C., June 1968). L-dopa in oral doses of up to 8 Gm a day had been given to 38 patients for periods of one to six months at the time the trial was reported. Improvement occurred in 28 (75 percent) of the patients. Most of the symptoms of parkinsonism were relieved to some degree, with greater improvement in akinesia and rigidity than in tremor. Patients were responsive to treatment regardless of the severity of the disorder. The optimum doses of L-dopa had to be determined by trial and error for each patient; the average daily dose required for continuing beneficial effects was 6 Gm a day. Medical Letter consultants have observed similar favorable responses in other studies which have not yet been reported. The side effects encountered in the Yahr study (cited above) and others have been essentially similar in frequency and severity to those observed in the Cotzias study (cited above). In all of the studies, only a few patients had to discontinue treatment because of adverse effects.

Current Status of L-dopa—How long the effects of L-dopa on the symptoms of parkinsonism can be maintained is not yet known. Nor is there any assurance that longer use will not elicit new and perhaps serious side effects. Nevertheless, this appears to be a drug that can make life tolerable and reasonably normal for many patients who are now disabled by the disease, and many such patients would gladly take whatever risks are involved in the use of L-dopa. Fortunately, efforts are being made to speed the advance of the drug from the investigational to the marketing stage. The National Institutes of Health and the Parkinson's Disease Foundation are now taking responsibility for increasing the number of studies in clinical research centers so that the Food and Drug Administration will have enough data when it acts on a new-drug application for marketing L-dopa. Physicians who are now using the drug in clinical investigations are under considerable pressure from other physicians to provide it for their patients, but use of the drug outside FDA-approved studies is not permissible. Even if it were, the number of patients (in the United States alone variously estimated at 300,000 to 1,500,000) far exceeds the available supply.

Anticholinergic Therapy—Until L-dopa becomes generally available, the treatment of parkinsonism must continue to depend primarily on drugs with central anticholinergic activity (Medical Letter, Vol. 7, p. 22, 1965); such drugs have very limited effectiveness in most patients. Among those commonly used are piperidines, such as Trihexyphenidyl Hydrochloride USP (Artane; Tremin; Pipanol HCl) and its analogues (procyclidine [Kemadrin]; cycrimine [Pagitane HCl]; biperiden [Akineton]). These drugs are similar pharmacologically and clinically, as well as in chemical structure. The bella-

donna alkaloids—atropine and scopolamine—are still used occasionally; their synthetic analogue, benztropine methanesulfonate (Cogentin), is used more frequently. In general, the synthetic anticholinergic drugs have the advantage of a higher ratio of central to peripheral anticholinergic activity than the natural alkaloids.

Other antiparkinsonism drugs with anticholinergic activity are the antihistamine diphenhydramine (Benadryl; and other brands), orphenadrine hydrochloride (Disipal), chlorphenoxamine (Phenoxene), and the aminoethyl phenothiazine derivative, ethopropazine (Parsidol HCl); they are used either alone or in combinations. There seems to be little reason to give preference to any one of these agents in starting therapy, but some patients apparently do better with some of these drugs than with others.

It is usually impossible to achieve an optimal drug response without accepting some untoward physical and mental effects. Doses of anticholinergic drugs must be adjusted if mental disturbances are to be kept within tolerable limits. Patients vary greatly in their susceptibility to adverse mental effects, but in general, older patients are the most likely to develop troubling symptoms with ordinary doses. Different drugs, singly and in combinations, and in different doses, should be tried in the search for effective therapy with tolerable side effects. In many instances the optimum balance of therapeutic and side effects will be found at doses recommended by the manufacturer, but in others, higher doses will be required.

Antidepressants—Amphetamines such as d-amphetamine, methamphetamine, and methylphenidate (Ritalin) have been used to combat the apathy and depression which frequently accompany parkinsonism. Monoamine oxidase (MAO) inhibitors such as isocarboxazid (Marplan), nialamide (Niamid), and phenelzine (Nardil) seem to relieve depression in some patients with parkinsonism. Amphetamines and other adrenergic agents should not be used together with MAO inhibitors since such use can cause severe hypertensive crises. Certain foods, such as meat extracts and aromatic cheeses, and other foods containing tyramine can also cause hypertensive crises in patients taking MAO inhibitors.

The tricyclic antidepressants, such as imipramine (Tofranil), desipramine (Pertofrane; Norpramin), nortriptyline (Aventyl), amitriptyline (Elavil), and protriptyline (Vivactil), have been reported to have beneficial effect on tremor and depression, probably as a result of their central anticholinergic and sympathomimetic action (R. R. Strang, Brit. Med. J., 2:33, 1965). Although convincing evidence of their value is lacking, they are now used by some clinicians in modest dosage (25 mg three times a day) in the treatment of parkinsonism. Daily exercise and other physical therapeutic measures should always accompany drug therapy for parkinsonism.

Surgery—Stereotaxic surgery, usually thalamotomy, has reduced tremor and rigidity in many patients, though often not permanently. Unfortunately, surgery does not appreciably alter the other disabling symptoms of parkinsonism, such as akinesia, festination, loss of equilibrium, postural abnormalities, and speech difficulties. If the results of further investigation of L-dopa are as favorable as those now reported, the need for stereotaxic surgery will be much less frequent.

Drug-Induced Extrapyramidal Reactions—Studies of the effectiveness of L-dopa in the treatment of tremor and other extrapyramidal symptoms induced by such drugs as the phenothiazines and reserpine have not yet been reported. Acute or early extrapyramidal reactions are usually completely reversed by discontinuance of the phenothiazine or other drug. Late extrapyramidal reactions may be irreversible and may fail to respond to anticholinergic drugs. Anticholinergic drugs frequently used to treat drug-induced extrapyramidal reactions include benztropine, biperiden, and diphenhydramine.

Conclusion—If further trials confirm the results of investigations thus far, L-dopa will provide far more effective therapy for the symptoms of parkinsonism than any previously available drug. Every effort should be made to speed further trials and, if the results continue to be favorable, the marketing of the drug.—The Medical Letter 10(18), Sept 6, 1968.

ERRATA

Correction of item under "Did You Know" page 25 of *U.S. Navy Medical News Letter* of 5 July 1968.

Rear Admiral Alfred W. Chandler, DC USN, Ret, noted that the assertion stating the United States recently changed its territorial water claim from 3 to 12 miles was in error. The sentence should read "The United States territorial sea claim is 3 miles, but the fishing limits were recently changed to 12 miles."

☆ U.S. Government Printing Office: 1968 — 341-715/7